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WOUND HEALING IN ANTERIOR GASTRO-ENTEROSTOMY FOLLOWING VARIOUS METHODS OF SUTURE

AN EXPERIMENTAL STUDY IN DOGS

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Our primary object in this study was to ascertain whether serosal inclusions or cysts, such as are found not infrequently on the posterior parietal pelvic peritoneum, on the female pelvic viscera and elsewhere, would form on apposed serosal surfaces as in the case of gastro-intestinal anastomoses. As our work progressed, some of our observations were apparently so singular that we also became interested to know how wound healing following gastro-enterostomy progressed after the use of some of the suture methods most commonly practiced in this country and recommended by textbooks of surgery.

The latter generally advise one of three procedures for the closure of the so-called anterior ostial defect in gastro-enterostomy wounds: an ordinary continuous catgut suture [1] passed through the entire thickness of stomach and intestinal wall (fig. *2B*); a Connell stitch [2] (fig. 1*A*), which is a continuous mattress suture that has its loop on the mucosal aspect of the stomach and intestine, or a so-called baseball stitch (fig. 1*B*) (Schmieden suture).[1b] It is noteworthy that some authors [3] recommend that, for the purpose of hemostasis, the *mucosa be turned*

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1. (*a*) Da Costa, J. C.: Modern Surgery, Philadelphia, W. B. Saunders Company, 1925, pp. 1083 and 1085. (*b*) Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, 1929, vol. 6, chap. 6, pp. 47 and 84; chap. 12, pp. 32, 40, 46, 50 and 56. (*c*) Moynihan, B.: Abdominal Operations, ed. 3, Philadelphia, W. B. Saunders Company, 1918, vol. 1, p. 186; ed. 4, 1928, vol. 1, p. 396.

2. Da Costa (footnote 1). Lewis (footnote 1). Moynihan (footnote 1). Connell, M. E.: An Experimental Contribution Looking to an Improved Technique in Enterorrhaphy, Whereby the Number of Knots is Reduced to Two, or Even One, M. Rec. **42**:335, 1892.

3. Lewis (footnote 1). Moynihan (footnote 1).

outward and not inward when placing the first anterior row of gastro-enterostomy sutures, while others recommend that no effort be made to invert the free edges. Others are of the opinion that the type of suture method or the kind of suture material used probably makes little difference in the operative result. It is also common practice among some operators, who use clamps to hold stomach and intestine in place while doing a gastro-enterostomy, to excise the mucosa that everts from the cut anterior gastro-intestinal margins. This excision is done by some with the cautery. A consideration of the various other suture methods and the utilization of variously prepared suture materials as employed in this country would lead one far afield. However, the conclusion is inescapable that suture methods and materials as employed by some are unsatisfactory in the opinion of others, but an explanation is not forthcoming.

A review of the literature reveals astonishingly little experimental work on suture methods in an operative procedure so commonly and yet so variously performed. The observations of Mall,[4] while concerned only with the study of healing of intestinal anastomoses, are so fundamental and in some respects so pertinent to this study that they will be referred to later. Flint's [5] excellent paper is the only one that we have been able to find in the English language that concerns itself with a histologic study of wound healing in gastro-intestinal anastomoses. Flint's work was done on dogs, and his histologic study is most detailed. Anterior gastro-enterostomies were performed by one of three suture methods: (1) a two tier method employing interrupted silk sutures for each row; (2) a three tier method, the Wölfler technic, employing a continuous chromic catgut suture for the mucosa, a continuous silk or linen suture for the seromuscular layer and a serosal suture of interrupted silk or linen; (3) a two tier method consisting of an innermost continuous catgut suture and an outer layer of interrupted silk similar to our method 5. Flint found that the healing time following the use of these methods is approximately the same and that the mucosa is healed at about fourteen days, while at twenty-three days the mucosa over the operative defect is normal in places and the muscularis mucosae is partially regenerated.

Further reference to Flint's observations will be made later; however, his general conclusion is that, because of the incomplete mucosal healing before the fourteenth day following gastro-enterostomy it is of practical importance to keep the patients on a "light diet." It is also our impression that Flint's primary interest was more the study of wound healing than a determination of differences following various

4. Mall, F.: Healing of Intestinal Sutures, Johns Hopkins Hosp. Rep. **1**:76, 1896.

5. Flint, J. M.: The Healing of Gastrointestinal Anastomoses, Ann. Surg. **65**:202, 1917.

suture methods, for he did not mention the suture method employed when he described sections that showed certain unusual phenomena.

Gould [6] did not describe the suture technic employed in his experimental gastro-enterostomy studies, and one is not able to infer from his text whether there was a difference in healing following various methods of suturing. In general, the average time for mucosal healing was given as fourteen days. He stated [7] that on the tenth day a single line of cells starts across *from the stomach* and rapidly crosses the floor of the ulcer (the mucosal defect at the site of anastomosis).

The next histologic study that we encountered was by Gara.[8] In his experiments rabbits' stomachs were sectioned and then sutured by one of three methods: (1) a two tier method probably similar to our method 5; (2) a three tier method similar to our method 6, and (3) a method of his own which everts the sectioned tissues with the object of protecting the edges of the wound from the action of gastric juice. He claimed the best results with his method in that mucosal healing occurred in from one to two days. The three tier method, he stated, produces a smaller defect than the two tier method, but with both, contrary to our findings, he found mucosal healing incomplete in twenty-one days. Gara's report is inconclusive in that he described neither the suture material, the type of stitch nor the number of animals used in his experiments.

Klose and Rosenbaum-Canné [9] studied healing of wounds made with the cautery or scalpel in the stomach of sixteen cats. The wounds were sutured anteriorly only by one of three suture methods: (1) a one row serosal suture similar to our method 4; (2) the two row method of Czerny, and (3) the anterior inverting suture of Schmieden similar to our method 3. They killed their animals ten, twenty and thirty days after operation and found complete epithelization by the tenth day, following the use of the Schmieden suture. Epithelization was not complete after twenty days following the one row serosal suture method. The authors felt, however, that a two layer suture technic produces greater damage to the underlying structures than a single layer suture method; that cautery section produces much more inflammation and delayed union than knife section, and that although

6. Gould, A. H.: The Technic of Operations upon the Intestine and Stomach, Philadelphia, W. B. Saunders Company, 1906.

7. Gould (footnote 6, p. 23).

8. Gara, Max: Der Einfluss der Nahtmethode auf die Heilung operativer Kontinuitätstrennungen der Magenwand zugleich ein Beitrag zur Frage des Ulcus Pepticum jejuni postoperativum, Arch. f. klin. Chir. **120**:270, 1922.

9. Klose, H., and Rosenbaum-Canné, P.: Beiträge zur Magenchirurgie: I. Vergleichendexperimentelle Untersuchungen über die Magennähte, Arch. f. klin. Chir. **124**:15, 1923.

catgut as an inner row suture is absorbed, it produces considerable inflammatory change along the line of union as well as *marginal epithelial cysts.*

Kopyloff [10] studied gastro-enterostomy wound healing in sixty-one dogs following the use of five suture methods and the employment of various suture materials. He made observations also on the comparative rate of healing following scalpel, scissor and cautery incision, but did not study the comparative rate of healing following the use of various suture methods. He described, however, a ten day healing specimen from a gastro-enterostomy performed by means of a single layer of interrupted silk sutures (similar to our method 4) which showed epithelial union between the stomach and jejunum. The gastro-intestinal incision was made with a scalpel, and it was compared with another specimen in which a cautery was used and a mucous membrane defect was present after thirty days. He was in agreement with Klose and Rosenbaum-Canné that cautery incisions produce pronounced inflammation, thrombosis and delayed healing.

Kopyloff described "regenerative alveoli" in the mucosa at the margin of the previous operative defects as long as twelve months after operation. These are identical with the "marginal cysts" of Klose and Rosenbaum-Canné. He also described silk threads which migrated through the anastomatic site and lay in areas surrounded by epithelium that "resembles intestinal epithelium." These are identical with Mall's and our suture inclusions, and Kopyloff observed them in a three hundred and sixty-five day specimen. He did not describe mucosal inclusions in the line of apposition. Kopyloff, contrary to Klose and Rosenbaum-Canné, believes that the most rational method for gastro-enterostomy is a one layer serosal suture of fine catgut or interrupted silk (Lembert sutures) with a few interrupted catgut mucosal sutures at the angles of the anastomosis to maintain the size of the ostium. He unqualifiedly condemned continuous silk sutures and apparently was under the impression that all silk sutures eventually migrate into the gastro-intestinal lumen, while Lembert sutures migrate not through the line of apposition but at a point some distance from it. He gave no explanation for these phenomena, being evidently unaware of Halsted's fundamental studies [11] and the fact that his silk sutures migrate into the gastro-intestinal lumen because they are placed too deeply, piercing the mucosa.

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10. Kopyloff, G.: Über das Schicksal der Magendarm-Anastomose bei verschiedenen Nahtmethoden und bei einigen Modifikationen in der Operationstechnik, Arch. f. klin. Chir. **136**:568, 1925.

11. Halsted, W. S.: Intestinal Anastomosis, Bull. Johns Hopkins Hosp. **2**:1, 1891. Circular Suture of the Intestine, Am. J. M. Sc. **94**:436, 1887.

Nemiloff [12] reported histologic studies on gastro-enterostomy wounds in eight patients who died two, three, six, twelve, fourteen and twenty-four days, and in one instance nine months, after operation. A three layer technic using continuous silk was employed. A mucosal defect was noted in all the specimens up to and including the twenty-four day preparation. The nine months healing preparation showed complete mucosal healing and a silk thread in the line of anastomosis surrounded by mucosal glands. Nemiloff also observed dilated glands in the mucosa where it bordered the operative defect. *Restitutio ad integrum* was not observed, for definite scar formation was found underlying the regenerated mucosa.

The report of Strauch [13] is the most recent experimental histologic study that we have seen. Strauch used twelve dogs and ran two series of experiments. In one he sectioned the stomach transversely, and in the other he did anterior gastro-enterostomies and occluded the pylorus. The cut edges in both series were reunited by using several suture methods on the same specimen. In all experiments catgut suture material was used, and the dogs were killed at intervals of from two to forty-four days. Several suture methods were used: posteriorly (*a*) a single layer serosubmucosal suture which left the mucosa unsutured; (*b*) a two layer suture, one a serosubmucosal suture and the other a through-and-through suture of all the coats; (*c*) a two layer suture, one layer embracing the serosubmucosal structures and the other merely a so-called mucosal stitch, and (*d*) a three layer suture just as in our three layer method 6. Anteriorly, Strauch used three suture methods; (*e*) a two layer method, the innermost being a baseball (Schmieden) stitch similar to our method 3; (*f*) the everting method of Gara, and (*g*) a two layer method, the innermost being a continuous suture (Kürschner) involving all the coats and similar to our method 5.

Strauch concluded that suture methods *b, c, d, e,* and *g,* showed no marked differences in wound healing. However, with method *a* he found marked delay in healing owing to gaping of the mucosa, and he believes that any technic which does not bring the mucosal surfaces together delays healing. Strauch believes that posteriorly method *b* or *c* and anteriorly method *e* or *g* are the most desirable procedures. He did not describe marginal mucosal cysts or any type of epithelial inclusions.

We believe that the small number of animals used and particularly the simultaneous employment of several suture methods on the same animal present real defects in Strauch's experimental procedure.

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12. Nemiloff, A.: Ueber den Heilungsprozess in der Gastroenterostomiewunde, Arch. f. klin. Chir. **135**:629, 1925.

13. Strauch, C. B.: Histologische Untersuchungen ueber den Einfluss der Nahttechnic bei Magenoperationen auf die Heilung, besonders der Schleimhaut, Arch. f. klin. Chir. **137**:81, 1925.

PLAN OF STUDY

Forty-two dogs were used in two series of experiments for this study, twenty-two animals being employed in the first series and twenty in the second. The first series was completed and the histologic material examined before the second series was begun in order that observations made on the second might either confirm or refute the observations of the first series as chance occurrences incidental to some uncontrolled technical pitfall. Two animals died of postoperative complications, one (dog 20) dying on the table as the result of the anesthetic and the other (dog 54) of an infection of the upper respiratory tract thirty-four days after operation. Three specimens, from dogs 15, 20 and 27, were not used for study, so that our observations are based on thirty-nine animals.

Either an anterior gastroduodenostomy or a gastrojejunostomy was performed on each animal under ether narcosis and with customary surgical asepsis by the suture methods to be described. Water was given the animals as soon as they would take it. On the fourth day after operation, the day of operation being counted as one, milk and hamburger steak were added to the ration; on the sixth day the ordinary kennel ration, milk and dried horse meat, was given. It is obvious that no attempt was made to shield the gastro-intestinal wound from contact with coarse food.

The animals were killed by chloroform, six, nine, fourteen, twenty and twenty-seven days after operation. An autopsy was immediately performed. The distal two thirds of the stomach and the anastomosed intestine were removed with as little manipulation as possible and placed in a fresh diluted solution of formaldehyde U. S. P. (1:10). The specimens were not disturbed until fixation was complete; then blocks were taken by razor section from the midportion of the anterior and posterior anastomatic areas. Paraffin embedding was employed, and the sections were stained with hematoxylin and eosin.

SUTURE METHODS

Seven different suture methods were employed in this study and will be referred to by number rather than by a descriptive appellation. The suture materials were the same throughout, 00 plain catgut and 0 black silk. The finest curved intestinal needles were employed. In all our experiments stay sutures of silk were used, and the first posterior suture was a continuous serosubmucosal stitch of silk. Also, in all our experiments, the final anterior tier of sutures were Halsted serosubmucosal mattress sutures of silk.

Method 1 (Connell suture) was used only on the anterior aspect of the ostium, and consisted of a continuous through-and-through mattress suture of catgut with its loop on the mucosal aspect of the stomach and intestine, as shown in figure 1 *A*. This suture inverts the mucosa readily and, as previously noted, is a method described in some of the surgical textbooks. It was reenforced by a second row of Halsted sutures as already mentioned.

Method 2 was used only posteriorly. After the first posterior tier of silk was placed, the stomach and intestine were incised, and a second suture of continuous catgut was placed as a through-and-through lock-stitch or button-hole suture embracing the entire thickness of both walls. This suture was not used anteriorly because it formed (dog 15) a ridge of tissue so large as almost to prevent its peritonization by a second row of Halsted sutures.

Method 3 was used only on the anterior aspect of the gastro-intestinal ostium. It consisted of a continuous catgut suture passed from side to side alternately, the suture always passing from mucosa to serosa—a so-called baseball stitch (fig. 1 *B*).

This suture method, macroscopically at least, inverts the mucosa satisfactorily, without technical difficulty, and is one commonly recommended in some American textbooks. This suture line was, in turn, peritonized by a serosubmucosal row of silk Halsted sutures.

Method 4 (the Halsted presection method [14]) was used anteriorly only and employed a single row of presection Halsted sutures of silk. Hemostasis on the anterior aspect of the ostium was effected with free ties of catgut. When the presection sutures were tied, those intervals between them which required it were sutured with Lembert or Halsted stitches of silk (fig. 2 *A*). This method gives most excellent and ready inversion of the mucosa and is described in American textbooks only for use with the Finney pyloroplasty.[15]

Method 5 was used both anteriorly and posteriorly. It was used posteriorly as a second tier continuous catgut suture that passed through all the coats of stomach and intestine after they had been incised, and served as an effective hemostatic

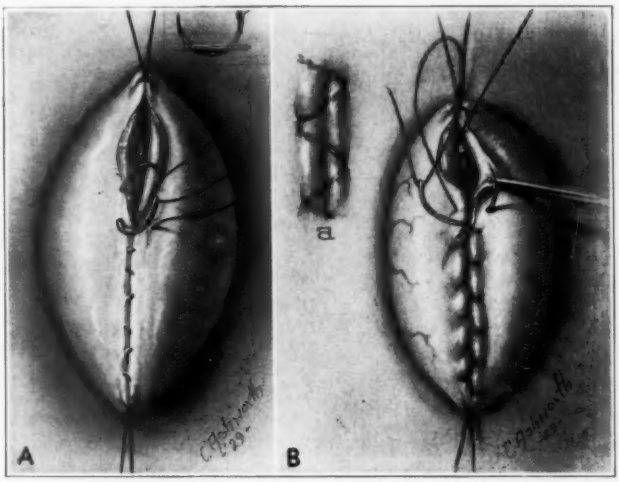

Fig. 1.—*A*, suture method 1, the Connell stitch, which is used only on the anterior aspect of the gastro-intestinal ostium. *B*, suture method 3, the so-called baseball stitch, which is used only on the anterior aspect of the gastro-intestinal ostium. Schematic illustration of suture is shown at *a*.

stitch. Anteriorly again it was used as a continuous catgut stitch that passed through all the coats of stomach and intestine and inevitably resulted in eversion of the mucosa and the formation of a ridge of tissue that at times was difficult to peritonize by the second tier of Halsted stitches. Figure 2 *B* illustrates this suture method, which is one strongly advocated and described in various textbooks of surgery.

Method 6 was employed both anteriorly and posteriorly. The first posterior tier of silk was placed as usual, and the stomach and intestine were incised down to the submucosa. A second suture of continuous catgut was then placed through

14. Halsted (footnote 11, first reference).

15. Finney, J. M. T.: A New Method of Pyloroplasty, Tr. Am. Surg. A. **20**: 165, 1902.

the serosa and muscularis of both stomach and intestine. Some submucosa was also included in this suture, care being used not to pierce the mucosa. The submucosa and mucosa were then incised and sutured with a third tier of continuous catgut. This last suture is often spoken of as a mucosal suture. However, mucosa will not withstand even the slightest suture tension, so that some submucosa must be included. The anterior sutures were then placed by continuing the third posterior row to form the first anterior row, which included only mucosa and submucosa. The second posterior row was continued to form the second anterior row of continuous stitches, which on the gastric side included muscularis and submucosa and on the intestinal side, owing to the thinness of the intestinal wall, muscularis and serosa. The third row of sutures was, as previously noted, of silk Halsted stitches. Figure 3 illustrates this method, which is one employed by numerous operators. It is effective for hemostasis and generally produces little mucosal eversion on the anterior aspect of the ostium.

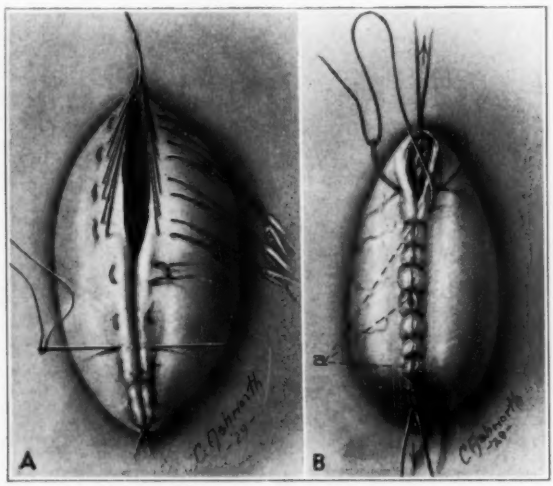

Fig. 2.—*A*, suture method 4, the Halsted presection suture technic, in which only one row of sutures is used on the anterior aspect of the ostium. *B*, suture method 5, an ordinary continuous suture, which is used both anteriorly and posteriorly. When used on the anterior aspect of the ostium, it inevitably causes macroscopic mucosal eversion, as shown at *a*.

Method 7 was employed both anteriorly and posteriorly in a third series of animals. In this report we shall describe only the results with the use of this suture posteriorly. The second posterior suture in this method is the same as that used for the second posterior row in method 6 (fig. 3). After being incised the mucosa was not sutured, hemostasis being effected by ligation of individual bleeding points.

This posterior suture is obviously ineffective for hemostasis. We were interested, however, in comparing the healing process following this suture method, which did not suture the two mucosae together, with the other posterior methods, viz., methods 2, 5 and 6, for it seemed to us that probably one of the sutures used in the three tier method was superfluous. The use of this suture on the anterior aspect of the ostium will be reported in another paper.

HEALING OF THE ANTERIOR ASPECT OF GASTRO-ENTEROSTOMY WOUNDS

Our primary interest in this study was the observation of wound healing. It was essential, therefore, that our specimens be obtained with the least possible manipulation at the time of autopsy and that undisturbed fixation be permitted before the specimens were cut. As a consequence, observations as to the size of the gastro-intestinal ostium had to be estimated on hardened tissue, and we therefore doubt their value. It can be said, however, that in so far as the diameter of the ostium was concerned, it measured 3 cm. in our smallest specimen and 6 cm. in our largest, the average being about 4 cm. In other words, even in the fixed specimens the ostia were adequate in size, but they

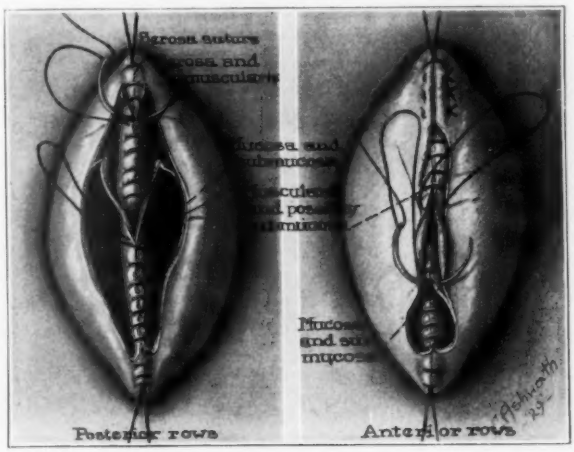

Fig. 3.—Suture method 6, a three layer method, which is used both anteriorly and posteriorly.

probably do not reflect in any accurate way the condition in vivo when one stops to consider the extensive and rapid change in size to which stomach and intestine are susceptible.

In preference to the foregoing, we measured the depth of the inner flange in the belief that this would give us some necessary information as to the comparative narrowing of the smallest ostial diameter caused by the various suture methods. These results will be summarized, as will our observations on the occurrence of adhesions. The following observations are confined to histologic detail and are here given only in briefest outline. No attempt is made to go into minute histologic description, for the meticulous descriptions of Mall and of Flint adequately portray the general process of the healing of intestinal and gastro-intestinal wounds.

METHOD 1 (Connell Suture).—Nine dogs (9, 11, 12, 13, 14, 32, 37, 42 and 47) were killed as follows: Two on the sixth day, two on the ninth day, two on the fourteenth day, two on the twentieth day and one on the twenty-seventh day.

Six day specimens (14 and 37) showed a well defined defect on the mucosal aspect at the point of stomach and intestinal apposition. Here there was a flat depression covered over by a fibrinocellular membrane, beneath which was a broad zone of young granulation tissue that extended into the submucosa for a short distance. Beyond this, where the serosal aspect of stomach and intestine had been apposed, one saw a broad zone of fibrous stroma with some round and polymorphonuclear cell infiltration and some capillaries. About the catgut sutures in the intestinal wall was a compact polymorphonuclear cell infiltration which was actually an abscess that extended out to the mucosa. Here the intestinal glands showed characteristic dilation and distortion due to the suture trauma.

On the gastric side also was seen mucosal gland distortion and nuclear pyknosis where the catgut had pierced its substance, but here there was much less cellular infiltration.

On the gastric side of the mucosal defect were seen a few dilated glands which we have termed marginal cysts. These, as will be seen, were rather characteristic of the reaction of gastric and intestinal mucosa to trauma. The gastric mucosa showed varying degrees of cellular infiltration and edema up to and slightly beyond the point of the catgut suture defect. Parietal cells extended to within eight to ten gland-breaths of the mucosal defect.

On the intestinal side the tips of the villi showed the most outstanding evidence of injury. In many areas they had undergone complete degeneration. Others showed only partial degeneration with marked enlargement and cellular infiltration. This often extended well beyond the area of suture injury. The advancing epithelial margin of the mucosal defect on the intestinal side showed at times a layer from 2 to 3 cells thick; again one saw a single layer of cuboidal epithelium which became low cuboidal or flat in the most advanced 2 or 3 cells. Secretion globules were seen in some of these cells almost up to the most terminal cell of the advancing margin.

No serosa cells were seen in the line of apposition. The muscularis mucosae showed considerable distortion for a short distance from the mucosal defect. The muscularis on both sides showed marked distortion, with some cellular infiltration for the entire extent of the apposed area. Here and there some degeneration was seen.

The silk sutures showed well defined fraying and were embedded in a loose matrix of short spindle-shaped cells with a few large round cells. Some sutures had a moderate polymorphonuclear cell infiltration about them, while others showed no cellular type of reaction. The serosa proper showed a moderate granulation tissue reaction.

Nine day specimens (9 and 32) still showed a well defined, though smaller, mucosal defect covered by a pyogenic membrane. There was excellent fibrous union along the line of apposition, and probably there was less cellular infiltration than in the six day preparation. The specimen from dog 32 showed a well defined mucosal inclusion (fig. 4) near the serosa on the intestinal side of the anastomosis. This was lined by columnar epithelium with oval, basally situated nuclei; secretion globules were common. These and other inclusions will be discussed later.

Fourteen day specimens (11 and 42) showed a moderate mucosal defect in dog 11, while in dog 42 epithelium covered the site of apposition of stomach and intestine (fig. 5). Here there was incipient gland formation. Elsewhere along

the line of apposition out to the serosa there were varying degrees of cellular infiltration, most marked in dog 11, through a zone of compact fibrous stroma.

Twenty day specimens (12 and 47) showed a moderate mucosal defect in dog 12, while in dog 47 mucosal union was complete and showed gland formation. In both specimens there were varying degrees of cellular infiltration in the line of apposition. In some sections from dog 12 there was some hemorrhage which had separated histologically the two infolded surfaces.

A twenty-seven day specimen (13) showed mucosal union complete without gland formation. Union along the inner three fourths of the line of apposition

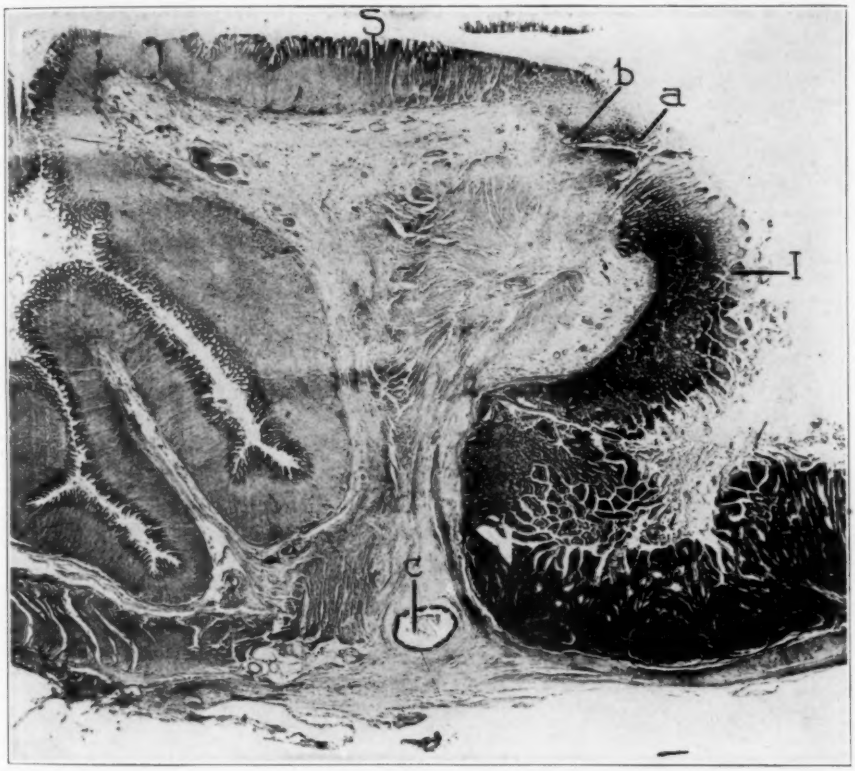

Fig. 4.—Dog 32, anterior method 1, nine day healing: *a*, site of mucosal defect with a granulation tissue mound; *b*, marginal cyst on the gastric side of the mucosal defect; *c*, suture inclusion near the serosal aspect on the intestinal side of the line of apposition; *I*, intestinal mucosa; *S*, gastric mucosa.

was rather loose, and varying degrees of cellular infiltration existed. There was no fresh granulation tissue. Healing near the serosal aspect was firm.

Summary.—The outstanding observations following the use of the Connell suture were the persistence of evidence of active inflammation in the line of apposition up to twenty-seven days after operation and also, in one specimen, evidence of hemorrhage and loose union. Mucosal healing occurred first at

fourteen days, and a mucosal inclusion in the wall of the intestine was observed once. In general, appositional healing appeared firm.

METHOD 3 (Baseball Stitch, Schmieden Suture).—Seven dogs (16, 17, 18, 19, 34, 38 and 43) were used and were killed as follows: two on the sixth day, two on the ninth day, two on the fourteenth day and one on the twentieth day. Six day specimens (16 and 34) showed a well defined mucosal defect (fig. 6), a pronounced cellular infiltration from mucosal to serosal aspects and well developed compact granulation tissue along the line of apposition. Nine day specimens (17

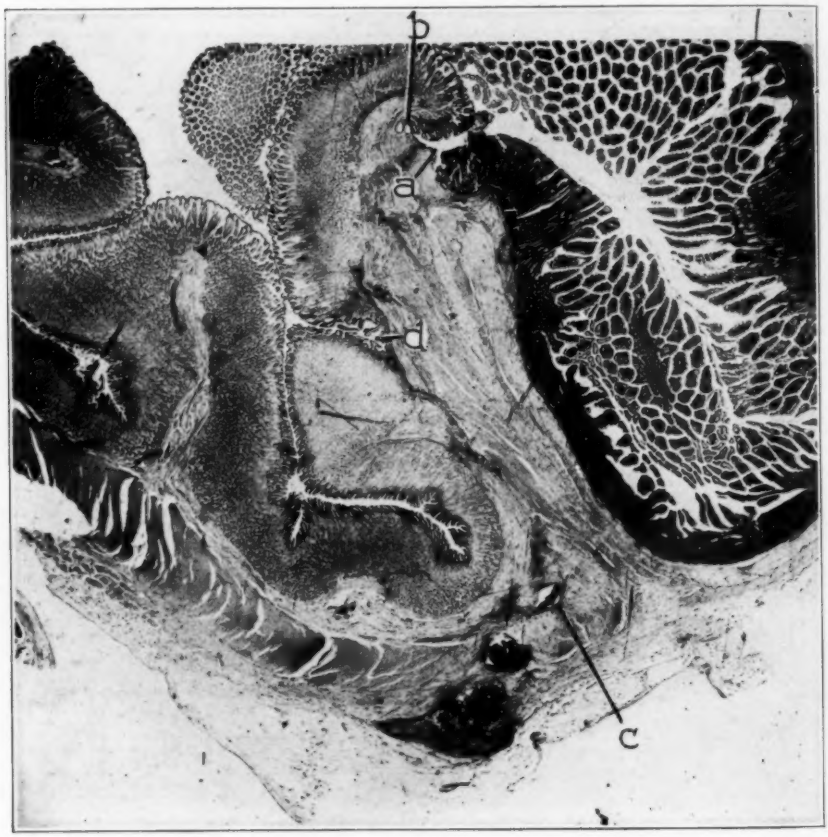

Fig. 5.—Dog 42, anterior method 1, fourteen day healing: *a*, site of the mucosal defect covered with a single layer of columnar epithelium; *b*, marginal cysts on the gastric side of the previous mucosal defect; *c*, silk sutures in the wall of the stomach; *d*, place where the catgut suture pierced the wall of the stomach. Excellent healing along the line of apposition.

and 38) showed mucosal union complete without gland formation in dog 17, while dog 38 had a well defined defect. There was a marked cellular infiltration from mucosal to serosal aspects, and a compact zone of young fibroblasts occupied the line of apposition. Fourteen day specimens (18 and 43) both showed complete mucosal healing with gland formation and little evidence of inflammation at the

site of union. Mucosal inclusions were seen in the line of apposition in both specimens. This was especially marked in dog 43, as is shown in figure 7. This inclusion resembled intestinal mucosa in that its epithelium, containing mucous globules, was columnar, with coarsely granular basal nuclei, and had the tinctorial properties of the intestinal mucosa. The glands were tubular with a cellular interglandular stroma, and there was some exudate in the lumen of the inclusion. These inclusions in the line of gastro-intestinal apposition have been previously described by us,[16] and will be considered more fully later in this paper. A twenty day specimen (19) showed complete mucosal union without gland formation and

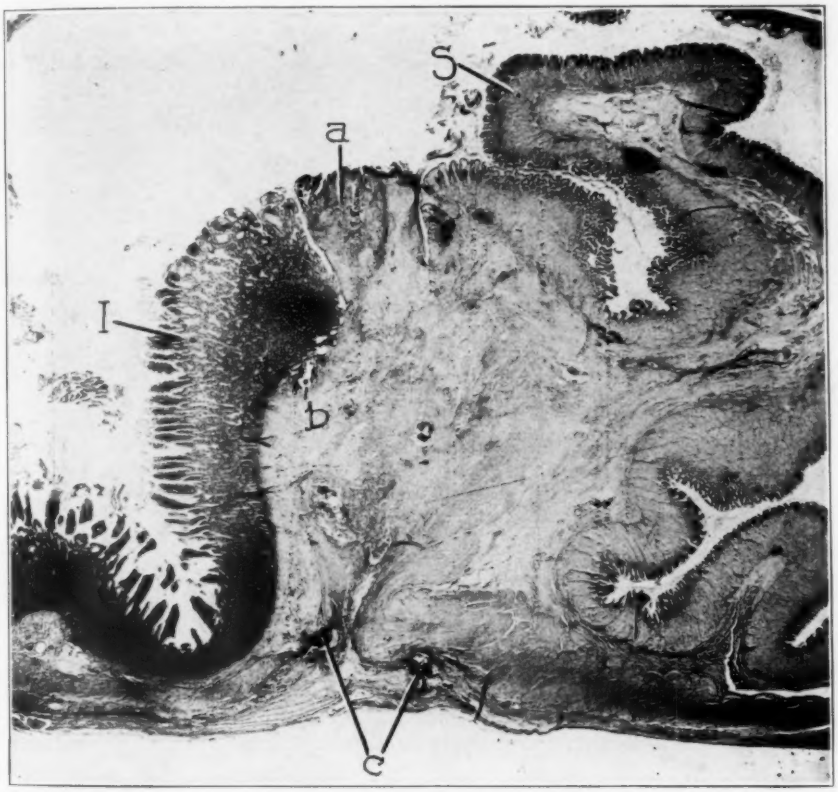

Fig. 6.—Dog 34, anterior method 3, six day healing: *a*, plateau-like granulation tissue material covered by a fibrinocellular membrane at the site of the operative mucosal defect; *b*, dilated intestinal glands, indicating place where the through-and-through catgut suture pierced the intestinal wall; *c*, silk sutures showing some fraying, a moderate round cell infiltration and a well defined surrounding hyaline change. Pronounced acute inflammatory reaction in the line of apposition. *I*, intestinal mucosa. *S*, gastric mucosa.

16. Martzloff, K. H., and Suckow, G. R.: Mucosal Inclusions in Anterior Gastroenterostomies in Dogs Following Various Methods of Suturing, Proc. Soc. Exper. Biol. & Med. **27**:855, 1930.

a mucosal inclusion in the line of apposition. Otherwise there was good fibrous union, with little evidence of cellular infiltration.

Summary.—Most of these histologic preparations showed considerable inflammatory change, not described in the individual protocols, in the mucosa of the stomach and intestine at some distance (from 0.5 to 1 cm.) from the line of apposition. Usually mucosal deformities could be seen which indicated the place where a catgut suture had pierced the viscus wall. Inflammatory cell infiltration was marked at the site of anastomosis in all specimens up to and including the nine day preparations. One of four specimens obtained with six and nine day healing showed mucosal continuity reestablished over the site of anastomosis. *Mucosal inclusions in the line of apposition* occurred in three of the seven specimens. The

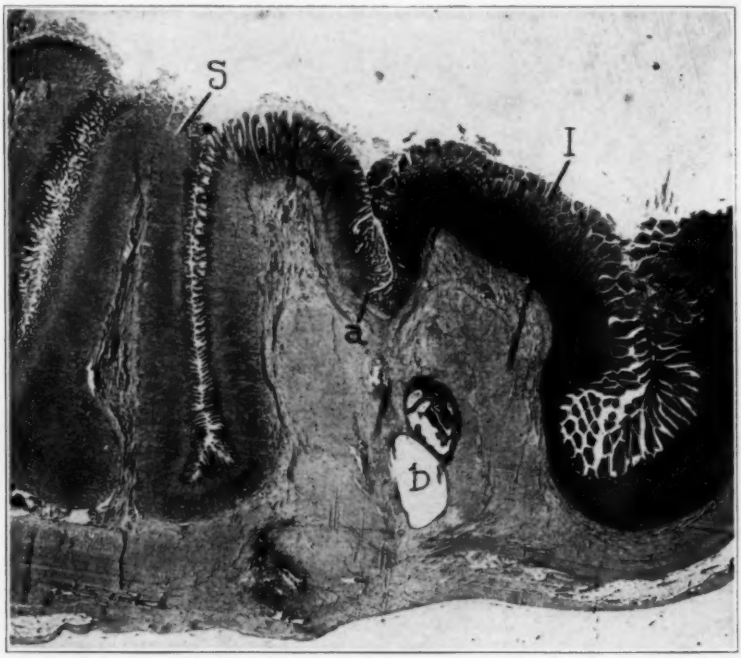

Fig. 7.—Dog 43, method 3, fourteen day healing: *a*, site of gastro-intestinal mucosal regeneration; *b*, mucosal inclusions (appositional rests) in line of apposition. The inclusion above *b* resembles intestinal mucosa. The mucosal epithelium is columnar; the nuclei are pyknotic and basally situated; many of the cells are distended with secretion globules. Inclusion *b* apparently shows evidence of distention, in that its walls are smooth and its lining epithelium is low cuboidal. There is well defined cellular infiltration along the line of apposition. *I*, intestinal mucosa. *S*, gastric mucosa.

healing of the mucosa and along the line of apposition in this suture method therefore surpasses that occurring in method 1. On the other hand, this method shows a high incidence of appositional mucosal inclusions.

Method 4 (Halsted Presection Sutures).—Seven dogs (21, 22, 23, 33, 39, 44 and 50) were used and were killed as follows: two on the sixth day, two on the ninth day, two on the fourteenth day and one on the twentieth day.

Six day specimens (21 and 33) showed complete mucosal union without gland formation (fig. 8) in dog 21, while in dog 33 healing was incomplete. Union along the line of apposition in dog 21 was remarkably free from cellular infiltration. There was a moderate granulation tissue structure beneath the mucosa, but elsewhere along the line of apposition no granulation tissue was seen, and there was very little round cell infiltration. In specimen 33 there was a well defined poly-

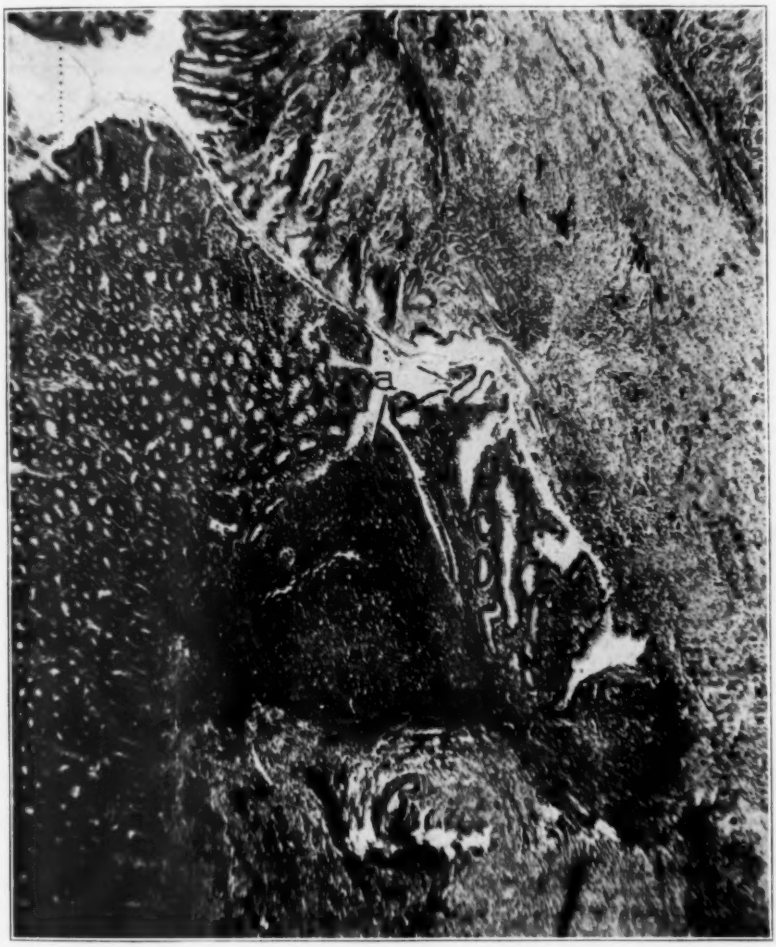

Fig. 8.—Dog 21, method 4, six day healing: *a*, site of operative damage to the mucosa, which is now covered with a single layer of columnar epithelium overlying an aggregation of round cells resembling a lymph follicle. Healing further out in the section, not shown here, is excellent, with a minimum of inflammatory reaction.

morphonuclear cellular infiltration at the mucosal defect, while further out in the line of apposition there were capillaries and fibroblasts with few accompanying round cells. Nine day specimens (39 and 50) showed complete mucosal union in

dog 50 (fig. 9), while a very small mucosal defect still persisted in dog 39. There was granulation tissue formation immediately beneath the mucosal defect in dog 39; otherwise both specimens showed very little cellular infiltration along the line of apposition. The healing in these two preparations was exceptionally free from evidence of inflammation and had the appearance of a firm union. Fourteen day specimens (22 and 44) showed complete mucosal union (fig. 10) with gland formation and a narrow, compact zone of fibrosis with practically no cellular infiltration along the line of apposition. These specimens showed the best fourteen day healing of any of our preparations. A twenty day specimen (23) showed complete mucosal and interstitial healing with practically no evidence of inflammatory reaction. The serosa over the anastomatic site appeared normal.

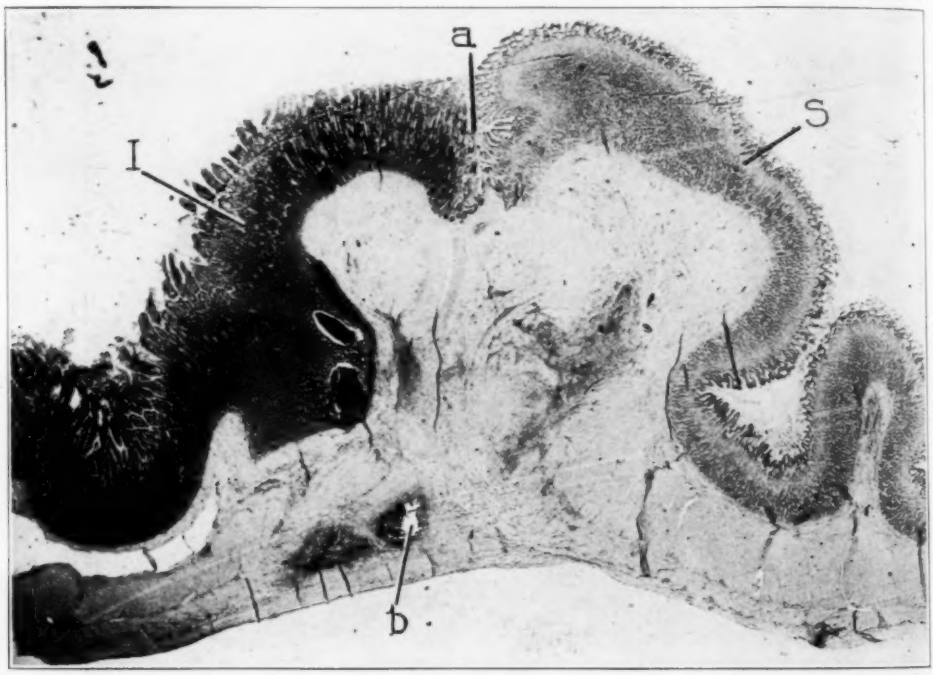

Fig. 9.—Dog 50, method 4, nine day healing: *a*, site of gastro-intestinal mucosal regeneration. Some loss of intestinal villi for a short distance to the left of *a*. Compact fibrosis along the line of apposition, with little round cell infiltration. Silk suture at *b*, to left of which there is an area of dense cellular infiltration, probably secondary to damage of the intestinal mucosa. Parietal cells of the stomach mucosa occur within from two to four gland-widths of regenerative defect. *I*, intestinal mucosa. *S*, gastric mucosa.

Summary.—Four of the six specimens obtained between the sixth and fourteenth days showed complete mucosal union. The specimens all showed remarkably little evidence of inflammation at the site of anastomosis, and no mucosal inclusions were seen.

Method 5 (Ordinary Continuous Suture).—Eight dogs (24, 25, 26, 35, 40, 45, 49 and 54) were employed and were killed as follows: two on the sixth day, one

on the ninth day, two on the fourteenth day, two on the twentieth day and one on the thirty-second day.

Six day specimens (24 and 35) showed most pronounced mucosal defects and an intense inflammatory reaction along the line of apposition. Large deposits of fibrinocellular material were present just beneath the serosa (dog 24), which strangely enough appeared virtually intact. In dog 35 (fig. 11) large open spaces, due to the dropping out of exudate, were seen in the line of apposition. Bits of mucosa were found well out in the line of apposition in dog 24. A nine day specimen (40) showed mucosal union incomplete, though only a small defect was

Fig. 10.—Dog 44, method 4, fourteen day healing. High power photomicrograph to show complete mucosal regeneration, with gland formation at *a*. The remainder of the section shows practically no inflammatory reaction along the line of apposition. *I*, intestinal mucosa. *S*, gastric mucosa.

left. There was a moderate degree of inflammatory reaction along the line of apposition, and here also a large *mucosal inclusion* was present. The latter, in some sections, was seen to communicate with the gastro-intestinal lumen. Fourteen day specimens (25 and 45) showed complete mucosal union with gland formation only in dog 45. Both had a well defined fibrosis and cellular infiltration along the line of apposition, while dog 25 showed a well defined mucosal defect covered with a fibrinocellular membrane. This same preparation showed a mucosal inclusion (fig. 12) extending well out in the line of apposition, while the specimen

from dog 45 showed a mucosal inclusion associated with a silk suture in the intestinal wall. Twenty day specimens (26 and 49) showed mucosal union with gland formation and mucosal inclusions associated with silk sutures on the intestinal side of the preparation. In addition, preparation 49 (fig. 13) had a large mucosal inclusion in the line of apposition, which we have previously reported.[16] Both specimens showed considerable fibrosis and cellular infiltration in the line of apposition. A thirty-second day specimen (54) showed a complete mucosal union with gland formation at the line of anastomosis, but a few millimeters from here there was extensive degeneration of the gastric mucosa. There was a large

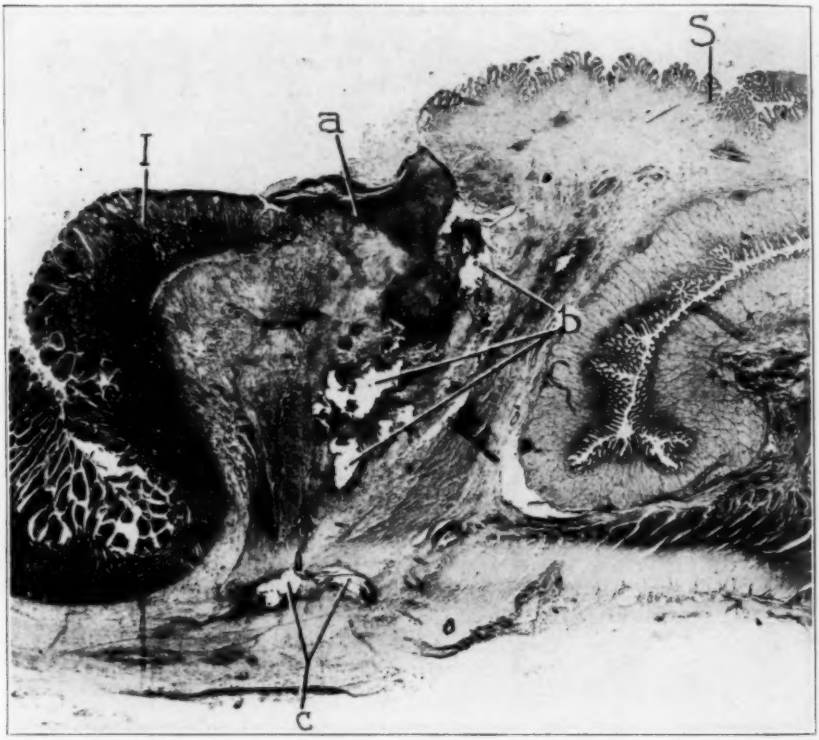

Fig. 11.—Dog 35, method 5, six day healing: *a*, broad granulation tissue plateau covered with a fibrinocellular membrane occupying the zone of the operatively produced mucosal defect; *b*, large spaces from which the exudate has dropped out. A profound inflammatory reaction in the line of apposition. Silk suture defects are shown at *c*. *I*, intestinal mucosa. *S*, gastric mucosa.

mucosal inclusion, associated with a silk suture, that involved the intestinal muscularis. The cyst was dilated and lined in part by a single layer of columnar epithelium. This animal was not intended for inclusion in this series. However, its premature death from pneumonia rendered it unsuitable for our third series, so we included it in this report.

Summary.—Four of five animals operated on with this suture method and killed on or before the fourteenth day showed incomplete healing of the mucosa.

All the specimens showed considerable evidence of active inflammatory reaction. This was particularly true of the early healing periods. Four of eight specimens showed mucosal inclusions in the line of apposition, while a similar proportion showed mucosal inclusions associated with silk sutures in the intestinal wall. One specimen contained both types of inclusions.

Fig. 12.—Dog 25, method 5, fourteen day healing: high power view from the mucosal aspect of a section showing mucosal inclusion in the line of apposition as *a*, which in some sections communicates with the gastro-intestinal lumen; *b*, a thrombosed blood vessel. This photomicrograph does not show a well defined mucosal defect with a pyogenic membrane that still persists.

METHOD 6 (Three Tier Suture Technic).—Eight dogs (28, 29, 30, 31, 36, 41, 46 and 48) were used for this method and were killed as follows: two on the sixth day, one on the ninth day, two on the fourteenth day, two on the twentieth day and one on the twenty-seventh day.

Six day specimens (28 and 36) showed large mucosal defects (fig. 14) with an overlying fibrinocellular membrane. There were marked cellular infiltration and a compact granulation tissue structure in the line of apposition. A nine day specimen (41) showed complete mucosal union in some sections (fig. 15), while others showed incomplete union. There were compact fibrosis and considerable cellular infiltration along the line of apposition, and here also a very small

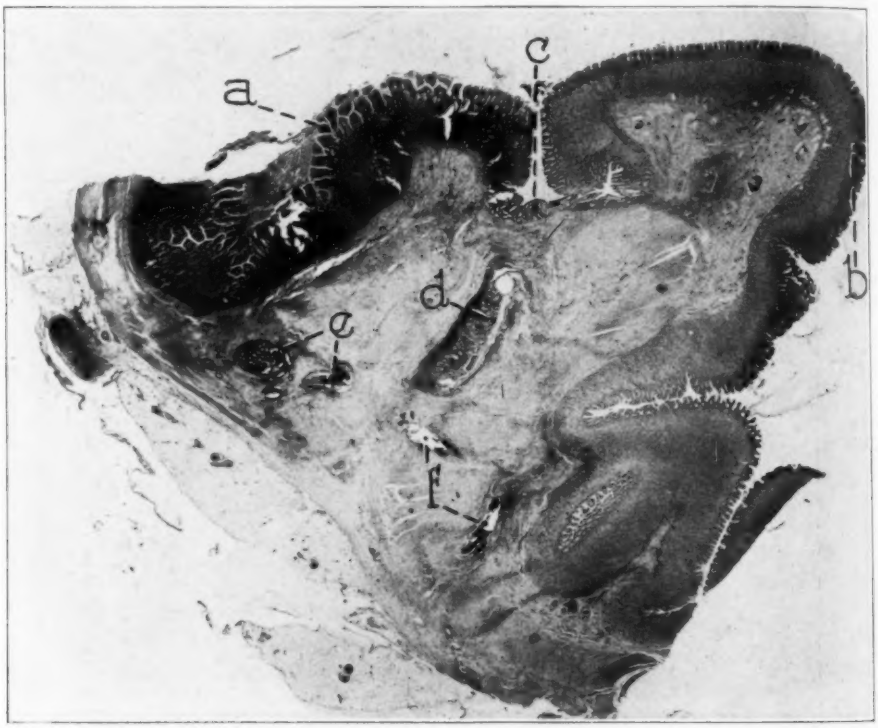

Fig. 13.—Dog 49, method 5, twenty day healing: *a*, intestinal mucosa; *b*, gastric mucosa; *c*, regenerated mucosal epithelium with gland formation at the site of a previous mucosal defect; *d*, appositional mucosal rest; *e*, suture inclusions on the intestinal side of the section, associated with a silk suture which lies in an epithelial lined space; *f*, silk suture defects.

mucosal inclusion was seen. Fourteen day specimens (29 and 46) showed mucosal union in the specimen from dog 46, while dog 29 still had a moderate defect covered with a fibrinocellular membrane. The line of apposition presented a compact fibrous structure with considerable cellular infiltration. There was a questionable mucosal inclusion in the line of apposition in specimen 29. Twenty day specimens (30 and 48) showed mucosal union with gland formation in specimen 48. In dog 30 there was so much round and polymorphonuclear cell

infiltration in the superficial one third of the intestinal mucosa that the gland pattern was almost wholly lost. There was a compact fibrosis along the line of apposition with moderate cellular infiltration in dog 48 and a more marked infiltration in dog 30, which also had a pronounced subserosal edema and round cell infiltration. A twenty-seven day specimen (31) showed mucosal union with gland formation over the line of anastomosis. This specimen also showed a pronounced inflammatory reaction involving the superficial portion of the gastro-intestinal epithelium.

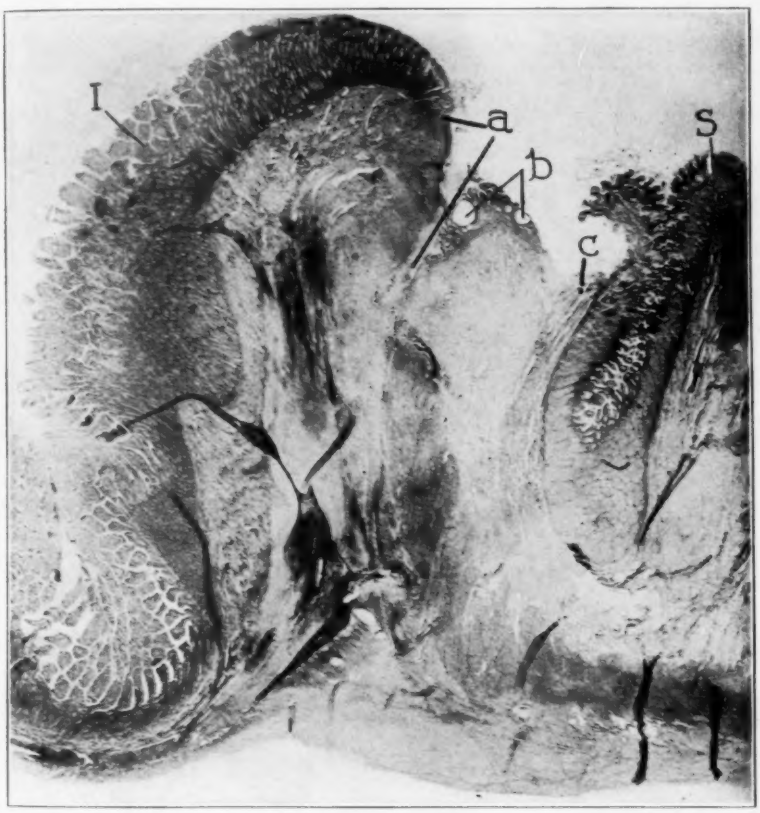

Fig. 14.—Dog 28, method 6, seven day healing: *a*, mucosal defect with granulation tissue and an overlying pyogenic membrane; *b*, marginal cysts on the gastric side of the defect; *c*, area devoid of mucosa owing to a technical artefact. Compact granulation tissue union along the entire line of apposition with well defined peritonitis on the serosa. *I*, intestinal mucosa. *S*, gastric mucosa.

Summary.—Mucosal union occurred in one, and partially in another, of five animals killed on or before the fourteenth day. Mucosal inclusions were definitely observed in one specimen, but they were so small as to be of questionable significance. Inflammatory reaction in the line of apposition and in the mucosa was an outstanding observation in the preparations obtained following this suture technic.

General Considerations: Mucosa.—Marginal cyst formation is the term used to designate the dilated glands seen in the mucosa where it borders the site of the operative injury. These mucosal cysts (figs. 4, 5, 14 and 15) were first described by Mall, and since then have been observed and described by others.[17] They were frequently observed in our specimens irrespective of whether mucosal healing was complete

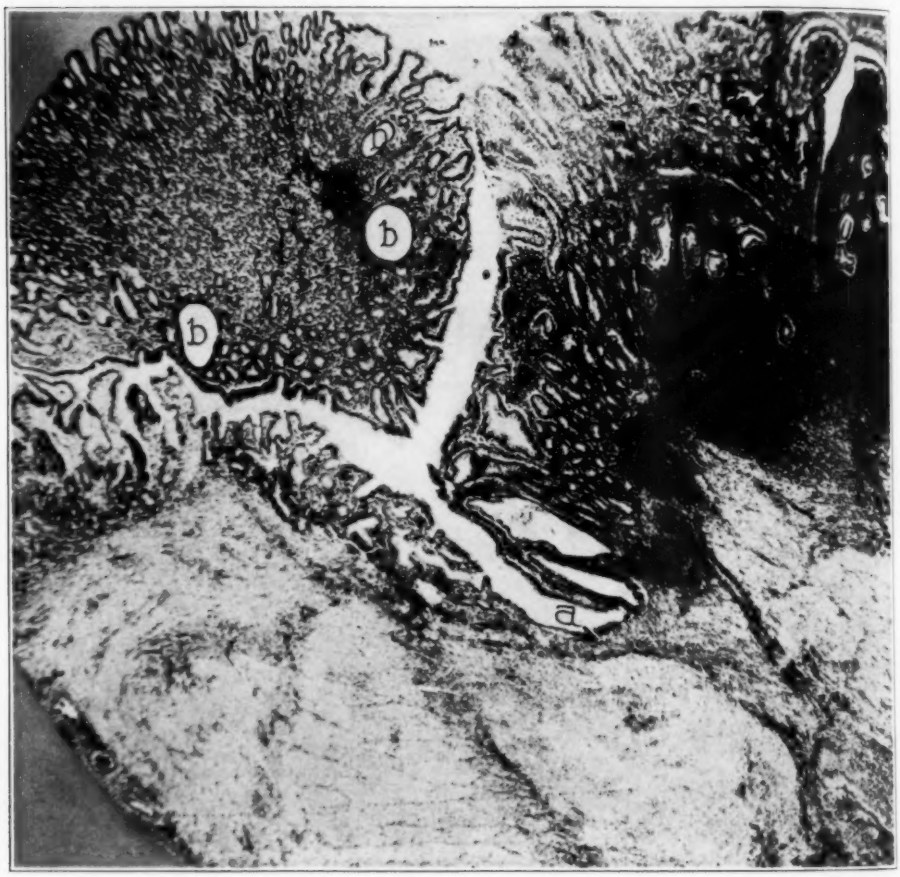

Fig. 15.—Dog 41, anterior method 6, nine day healing. This view is presented merely to show the excellent mucosal regeneration as a single layer of columnar cells without gland formation at *a* and marginal cysts at *b*. Other sections show incomplete mucosal healing. Further out in the section there is marked cellular infiltration in the line of apposition and a mucosal inclusion, which are not seen here.

17. Klose and Rosenbaum-Canné (footnote 9). Kopyloff (footnote 10) Nemiloff (footnote 12).

or incomplete. One of our specimens, to be described in another paper, showed marginal cysts after ninety days, and Kopyloff [10] observed them after twelve months. They were observed to occur on either the gastric or the intestinal side but most frequently on the former after any one of the suture methods that we have described. Since they occur after suture method 4, they are not necessarily due to suture trauma, as claimed by some.[9] Their cause has not been definitely proved; however, since they are generally lined by a single layer of flattened epithelium and have not been observed by us to communicate with the gastro-intestinal lumen, we believe that they are probably traumatic occlusions or retention cysts. Mall expressed the opinion that while these cysts are in part made up of remnants of crypts, they are mostly new-formed.

Mucosal Epithelial Regeneration: All our preparations were not suitable for the study of the advancing margin of the regenerating mucosal epithelium. Some sections, because of their size, were too thick to permit reliable interpretation, while others showed evidence of disturbance of the pyogenic membrane, which ordinarily covers the granulation tissue that bridges the mucosal defects.

Numerous sections, however, were suitable for the observation of the advancing epithelial margin over the mucosal defect at the site of the operative injury, and we present our observations for what they may be worth. In some specimens epithelium was observed growing over a granulation tissue matrix and beneath a fibrinocellular exudate, and in others it was seen to advance over a granulating surface free from exudate up to the point where the epithelium stopped. Epithelial regeneration appeared to come from the intestinal side as much as from the gastric side, and in this respect our observations are not in conformity with Gould's.[6]

Some specimens showed in the terminal 2 to 3 mm. of epithelium an abrupt tinctorial and morphologic change. This consisted in the newer cells becoming lower and broader and taking a lighter stain. Generally the cell outlines for a distance of from 1 to 3 mm. from the advancing margin were indistinct, and no evidence of secretory activity was seen. However, in one of our preparations evidence of secretory activity (intestinal) was seen right up to the point where epithelial proliferation ceases.

The advancing epithelial membranes were sometimes composed of a single layer of flat, cuboidal or low columnar cells in which mitotic figures were almost never observed. In some specimens (fig. 16) the advancing edge were from 2 to 3 cells high, while the individual cells were round and not flattened. We have also seen all the foregoing, except the columnar cells, under a pyogenic membrane. One of our

specimens (fig. 17) showed a distinct single layer of columnar epithelium on the intestinal side extending up to the epithelial margin where it began to go under a pyogenic membrane. This same specimen showed on the gastric side a single layer of flat epithelium growing beneath a pyogenic membrane.

It would seem, therefore, that, in so far as our observations are concerned, regenerating gastric or duodenal epithelium may assume a varied morphology.

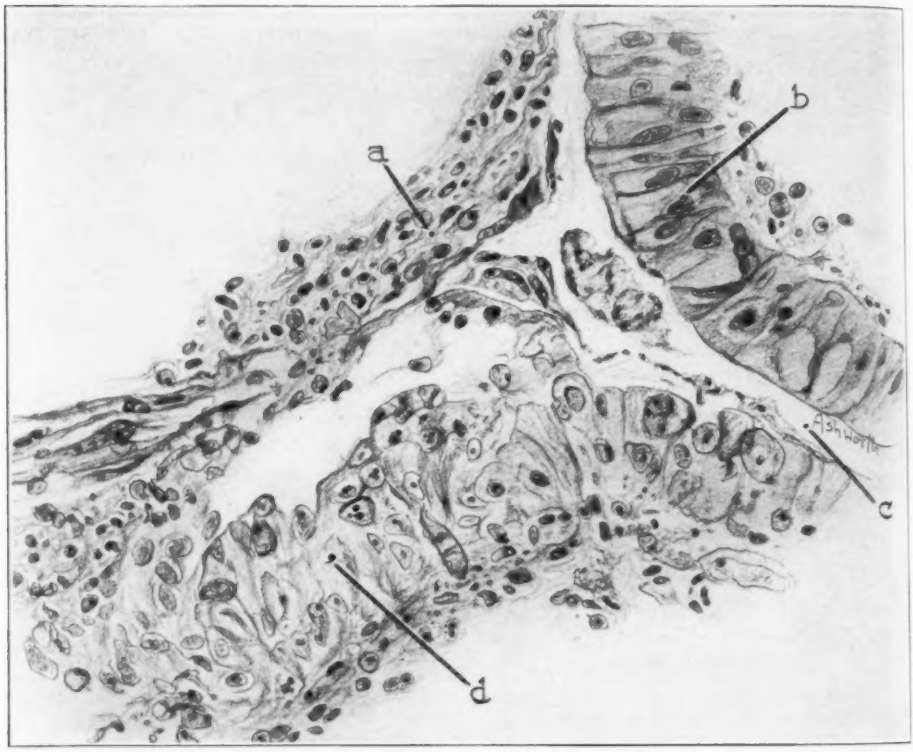

Fig. 16.—Dog 25. This drawing shows the advancing epithelial margin from the intestinal side at *d*, where the cells are several layers thick and round and oval in shape without any tendency to flatten, up to the point where they pass under a fibrinocellular membrane continuous with *a*. More or less normal intestinal epithelium is shown at *b*, and a crypt at *c*.

Gland Formation.—Gland formation in the mucosa covering the operative defect was not seen before the fourteenth day in any of our specimens. In the material from method 6 (three tier suture), gland formation in the area of repair was first observed in one specimen on the twentieth day. Although some specimens from all the other suture

methods employed showed gland formation on the fourteenth day of healing, it does not follow that all specimens with healing periods of twenty, twenty-seven or even thirty-two days, in which the same suture method was employed, showed gland formation in the area of repair. Gland formation as found in our material and also as observed by others appeared in its earliest stage as a mere dipping in of the epithelium into the underlying granulation tissue stroma.

Muscularis Mucosae, Submucosa and Muscularis.—The submucosa and the muscularis mucosae lose their identity entirely in the line of

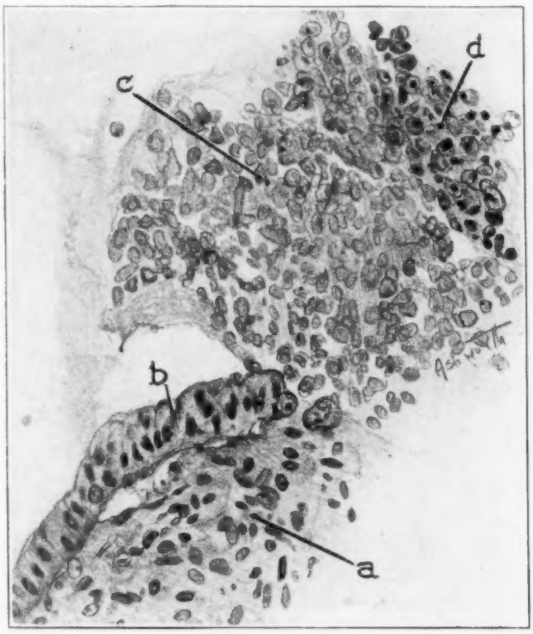

Fig. 17.—Dog. 9. Intestinal epithelial margin advancing as a single layer of cuboidal or low columnar cells (*b*) which retain their shape as they pass under a fibrino-red corpuscular area (*c*). The most distal cells have unrecognizable cell membranes. In some sections it appears as if the most advanced epithelial cells have secretion globules. At *a* are shown young fibrous stroma and at *d*, mononuclear leukocytes.

apposition because of the inflammatory process in the early stages of healing and because of scar tissue in the later stages. The longest period of healing observed in this study was thirty-two days.

The muscularis retains its identity during the entire healing process, but by no means does it remain intact. In the early days of healing, the involvement of its outermost layers in edema and cellular infiltration varies considerably with the suture technic used. Later the muscle fibers of stomach and intestine are joined by fibrous stroma, which was

not spanned by muscle fiber during the period of healing here observed. In other words no *restitutio ad integrum* was seen.

Serosa.—The serosal surfaces where they came in contact through the apposition of the stomach and intestinal walls lost their identity in all our specimens. Our observations do not permit an opinion as to how early the serosal cells lose their identifiability. However, we believe that our material shows that no recognizable serosal inclusions occur at the point where two comparatively broad serous surfaces are apposed.

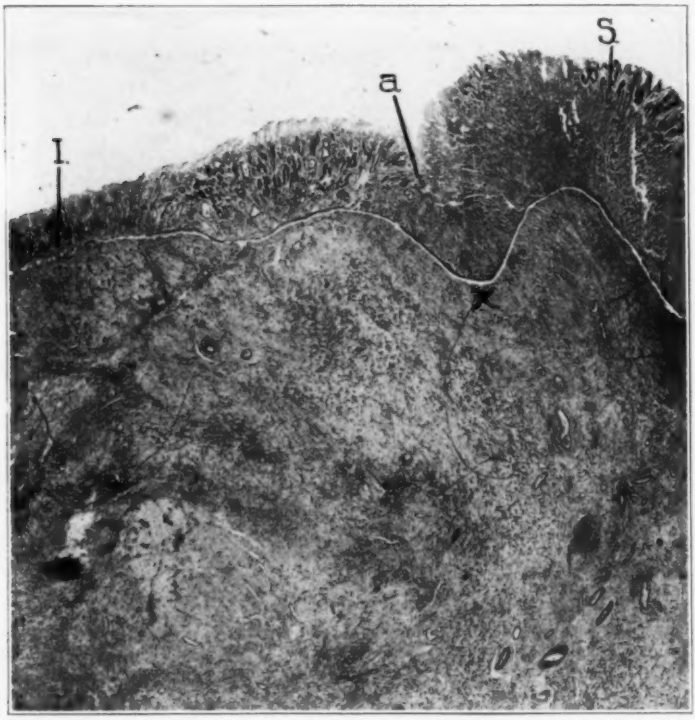

Fig. 18.—Dog 64, posterior method 7, six day healing. Remarkable mucosal restitution is shown at *a*, which extends to the line *x* drawn to show the boundary between the mucosa and the underlying stroma. Mucosa in area *a* shows distinct histologic alteration and does not resemble either intestinal (*I*) or gastric (*S*) mucosa. To the left of *a* is recognizable but altered intestinal mucosa with some dilated glands suggestive of marginal cyst formation. Healing further out in the section shows excellent fibrosis and little cellular infiltration.

This determination, among others, was one that this study was supposed to elucidate. Furthermore, we believe that the mucosal inclusions described by us in the line of apposition need not be confused with serosal cysts.

Mucosal Rests or Inclusions.—Reference to the illustrations and the brief protocols disclose that some of our specimens presented mucosal structures occupying one of two situations in the operative area; viz., (1) those found on the intestinal side of the anastomosis, generally in the intestinal wall nearer the serosa than the gastro-intestinal mucosal defect, and always associated with a silk ligature. These we have termed suture inclusions in contradistinction to (2) the mucosal rests which we found in the line of apposition between the walls of the stomach and intestine. These, for purposes of brevity, we have termed appositional rests.

Suture inclusions were observed in five specimens (figs. 4 and 13). Four of these were in animals in which suture technic 5 was used and the remaining one occurred with technic 1 (Connell suture). These inclusions, as shown in the illustrations, are all on the intestinal side of the anastomosis and are all associated with silk suture material. They may present a very simple gland structure, as in figure 4, or a more complex arrangement, as in figure 13. They are lined by a single layer of columnar epithelium which in places shows evidence of secretory activity, while mitotic figures are present. Their lumina generally contain a débris rich in polymorphonuclear cells, and there is considerable round and polymorphonuclear cell infiltration about the inclusions. In some preparations one can see evidence of damage to the intestinal wall near an inclusion that we interpret as being due to the inadvertent insertion of a silk suture into the mucosa at the time of operation. Due to pressure necrosis the suture cut its way through the mucosa, submucosa and a varying thickness of the muscularis, creating a defect along which the intestinal epithelium grew to form inclusions. These, therefore, are outgrowths which, in some specimens at least, communicate with the intestinal lumen to form small epithelial lined diverticula or sinuses. The evidence for this we shall present in another paper. In any event, these intramural glandular structures do not, as a rule, represent free grafts due to the transfer and implantation of isolated epithelial elements into the intestinal wall. The ultimate fate of these inclusions we do not know, but there is reason to believe [10] that they may persist indefinitely.

At first sight it may seem strange that such inclusions were encountered only in animals that were operated on by suture methods 1 and 5. The explanation is simple, in that with suture method 5 the tissues are so ridged at the line of apposition that it is difficult to place accurately the second row of silk Halsted mattress sutures. This results in an unintentional piercing of the intestinal mucosa in some specimens. Careless technic might easily produce the same formation in the other suture methods, which, however, afford conditions more suitable for the accurate placing of silk serosubmucosal sutures.

The nonoccurrence of analogous inclusions on the gastric side of the anastomosis is probably due to the greater thickness and toughness of the stomach submucosa, which thereby prevents the technical fault so easily committed on the intestine. Our experiments, however, do not definitely prove that gastric mucosa under similar circumstances would behave as the intestinal mucosa does. These inclusions have been observed by others [18] who, excepting Mall and Flint, gave them no consideration other than merely noting their presence. Mall,[4] however, is the first investigator to describe them and explain their origin as due to silk suture damage to the mucosal crypts. Mall also remarked that it is possible that these adenomatous structures "could do considerable mischief," but it appears that his original and beautifully accurate description, explanation and admonition have been largely overlooked.

Appositional rests, so-called, were observed eight times: in three specimens from suture method 3 (baseball stitch), in four specimens from suture method 5 (continuous stitch) and in one specimen from suture method 6 (three layer suture). Suture methods 1 and 4 were not complicated by these structures. It is noteworthy that these appositional rests occurred in methods in which sutures passed over free mucosal margins with resultant mucosal eversion. This fact is most marked with method 5. In method 6, eversion may also occur if the mucosubmucosal suture is not properly placed. Whether the catgut suture passing between the serous aspects of stomach and intestine in method 3 serves to act as a guide along which mucosa may grow, we cannot say. We have seen traces of catgut in the line of apposition in some of our six day specimens, but these were never associated with mucosal inclusions.

We do not believe that these appositional rests are due to mucosa growing along a zone of tissue damage produced by catgut as in the case of the so-called silk suture inclusions. If such were the case, laying aside all other considerations, one could expect to find some evidence of such a phenomena in suture method 1, in which sutures are passed directly through the entire thickness of stomach and intestine but without passing over the free inverted margin of either. It should be remembered that we are concerned here with 00 plain catgut suture material. These observations might not apply if a more durable variety of catgut were used. Some of our preparations showed areas of distinct damage to gastric and intestinal wall (including mucosa) by through-and-through catgut sutures, but in none of these did we see a suggestion of mucosal outgrowth along such a defect.

18. Flint (footnote 5). Kopyloff (footnote 10). Nemiloff (footnote 12).

We believe, therefore, that the mucosal inclusions found in the line of apposition of our specimens arose from mucosal displacement following eversion and were not directly related to suture transfixion of the mucosa. The mucosa of these inclusions generally had the appearance of intestinal mucosa, but our specimens and observations did not explain the absence of gastric mucosa in these rests.

The only references that we can find regarding these appositional mucosal inclusions are by Marchand,[19] Gould and Flint. Marchand illustrated a six day gastro-enterostomy specimen of Professor Küster's which showed approximately in the line of apposition and near the mucosal aspect, a small adenomatous structure which he said was due to sutures (silk) passed through the mucosa which caused some infolding. It may well be that in this specimen the silk may have been the cause of a suture inclusion. Gould had one illustration in his book which may probably be construed as a form of appositional inclusion, but which he considered the site of a former ulcer between the two mucosae. Flint in his excellent paper noted that tearing of the muscularis mucosae or its failure to regenerate allows crypts of the intestine to grow into the submucosa. At times these growths, according to Flint, occur at the site of the incision and penetrate for some distance into the submucosa and muscularis.

It is evident that the significance of these adenomatous structures has not been recognized. Certainly they do not invade muscularis and submucosa, but are merely transposed so as to lie between their cut ends. If any invasion occurs, it is purely a secondary process and then only in the nature of a concentric physical displacement and not a heterotopia as seen in a malignant condition.

We are now studying the ultimate fate of these inclusions.

Fate of Suture Material.—Catgut: Some of our six day healing preparations showed catgut which appeared as a hyaline substance surrounded by polymorphonuclear neutrophilic leukocytes. No catgut was observed in any of our nine or fourteen day specimens. No conclusion could be made concerning its rôle in the production of inflammation, for it was contaminated in all methods by its passage through the gastro-intestinal lumen.

Silk: The reaction of the tissues to silk varied considerably in different specimens. In some early preparations the silk sutures showed some fraying and were surrounded by a slight to moderate round cell infiltration with or without an occasional polymorphonuclear leukocyte. The round cells were of two varieties, one being the easily recognizable lymphocyte and the other a large oval cell with a pink tinge to its nucleus.

19. Marchand, F.: Der Process der Wundheilung, Stuttgart, Ferdinand Enke; Deutsche Chir. 1901, Pt. 16, pp. 300 and 306.

Some hyaline change was also observed in our six day healing specimens, while no giant cells were encountered in any of our material. In some of our older specimens as well as in an occasional six day specimen a hyaline reaction was about the only change noted about the silk sutures.

On the other hand, there were specimens both early and late in which every gradation from moderate cellular infiltration to frank abscess formation was seen about silk suture material. In fact some of the older preparations revealed practically no evidence of inflammation along the line of anastomosis until one arrived at a silk suture where a profound round and polymorphonuclear cell infiltration existed. These preparations generally showed evidence of damage to the intestinal mucosa where a suture was placed too deeply at the time of operation. Such findings were most common in suture method 5, and were not uncommon in the other suture methods except 3 and 4, in which they were also occasionally seen.

The explanation for these varied findings is probably merely a matter of surgical technic, and has been repeatedly stressed by Halsted. In preparations in which silk did not penetrate the mucosa, inflammatory reaction was minimal or virtually absent, while every degree of inflammation was observed when the mucosa was penetrated.

In suture methods 3 and 4, it was possible to place the Halsted silk mattress sutures so precisely that only occasionally was the mucosa penetrated. In the other methods, particularly method 5, the distortion caused by the first anterior catgut suture was, as previously noted, so pronounced that it was technically difficult to place the silk sutures accurately, with resultant penetration of the intestinal mucosa. Particularly is this true when one uses curved needles on a needle holder. Then, we believe, it is virtually impossible, as was first pointed out by Halsted [14] and recently experienced by one of us,[20] to "sense" the depth to which one's needle is penetrating, provided one is attempting to engage the outermost portion of the submucosa.

We are not able to state the ultimate fate of our silk sutures because our specimens, with one exception, were not over twenty-seven days old. Furthermore, our material was not studied primarily for this purpose, which would require some clearing method such as that employed by Reichert and Holman,[21] which would render it unsuitable for histo-

20. Martzloff, K. H., and Burget, G. E.: The Closed Intestinal Loop: III. Aseptic End-to-End Intestinal Anastomosis and a Method for Making a Closed Intestinal Loop Suitable for Physiologic Studies, Arch. Surg. **23**:26 (July) 1931.

21. Reichert, F. L., and Holman, E.: The Fate of Sutures as Observed in Intestinal Anastomosis and in the Healing of Wounds, Bull. Johns Hopkins Hosp. **36**:212, 1925.

logic study. We therefore report our observations for what they may be worth. In a few of our specimens we observed obvious migration of frayed silk particles toward the serosa, but none lying directly beneath it. None of our specimens, even those which had obviously damaged intestinal mucosa and were associated with mucosal suture inclusions, showed silk in the gastro-intestinal lumen. We do not infer from this that luminal migration does not occur, for it obviously does, as we shall be able to report in another paper.

In so far as our observations are concerned, it appears to us that 00 plain catgut is a satisfactory hemostatic suture; it is generally absorbed by the sixth postoperative day; while it does show histologic evidence of damage to the stomach and intestinal walls, where it transfixes them, the mucosal defects (not to be confused with the mucosal defect in the line of apposition) are healed by the sixth day; mucosa apparently does not grow along catgut defects as produced in our experiments; there is considerably more inflammation in suture lines when catgut is employed as we have used it than in methods that avoid its use.

We have made no experiments to see whether 00 plain catgut used as a serosubmucosal suture which penetrates the mucosa will give rise to mucosal suture inclusions.

Silk suture material, when fine and accurately placed, appears to us an ideal suture material in that it evokes practically no inflammatory reaction and permits almost primary healing. However, when silk suture material as used in our experiments is placed sufficiently deeply to penetrate the intestinal mucosa, it becomes involved in varying degrees of inflammatory reaction and in some instances is associated with mucosal inclusions.

The size of the gastro-intestinal ostia, as previously noted, could not be accurately studied in view of the fact that the fresh material was immediately fixed with the minimum of manipulation. The fixed specimens when sectioned, however, showed ostia the greatest dimensions of which varied considerably because of variation in the size of the animals used. None of the ostia was less than 2.5 cm. in length. The amount of inturned stomach and intestine varied according to the time after operation and the suture method used. The specimens removed six and nine days after operation showed much more of an inturned flange than those removed later. In fact the main difference between the flange of a six day healing and a twenty-seven day healing specimen was not so much the depth of the flange (from serosa to mucosa) as its width, which was greater in the early specimens owing to edema and cellular infiltration, which generally was least pronounced in suture method 4 (presection technic). In any event, the determination of inturned flange is not exact, for the same operator repeating the same operation must vary somewhat the amount of tissue that he turns in.

Gross evidence of hemorrhage from the free inturned portion of the gastro-intestinal wall was not observed in any of our specimens. However, one twenty day specimen (12) from suture method 1 (Connell technic) showed the lines of apposition almost completely separated by hemorrhage in some sections.

Serosal Adhesions.—Serosal adhesions at the site of operation were observed in all our early healing specimens. They varied considerably, and were never the cause of complications; we thought that probably they were most pronounced with suture method 5. However, after going over our material again, we rather doubt the correctness of this conclusion. A review of this particular point in a third series not included in this report shows that after ninety days only a few filmlike avascular adhesions remained in animals on which suture method 5 was employed.

HEALING OF THE POSTERIOR ASPECT OF GASTRO-ENTEROSTOMY WOUNDS

As will be noted in the illustrations, only two types of suture technic were employed on the posterior wall of the gastro-enterostomy ostium: (1) a two layer method (suture method 2), employing a sero-submucosal continuous 0 black silk suture and an inner row continuous lock-stitch suture of 00 plain catgut that passed through all coats of the stomach and intestine; (2) a three layer method (posterior method 6), in which the previously described sutures were all continuous.

We did not study the posterior ostial healing in all our specimens because of the many duplications.

Six to Nine Day Healing.—In four specimens in which the lock-stitch suture was employed, only one specimen (six days) showed the mucosal defect almost completely covered by regenerated epithelium. All four of these specimens showed marked inflammation in the line of apposition, and one showed considerable hemorrhage. One specimen showed a silk suture directly in the line of apposition and the site of abscess formation.

In three specimens in which the three layer method was employed there was excellent fibrosis along the line of apposition with a moderate cellular infiltration. In one (nine day) specimen epithelium covered the site of the mucosal defect, while the other two showed a granulating ulcer at the site of operative injury to the mucosa. In all seven specimens in which silk sutures were visible they appeared to be working their way toward the lumen.

Fourteen Day Healing.—One specimen in which the three layer method was used showed epithelial regeneration with gland formation. The healing along the line of apposition was excellent, showing a compact fibrous stroma with a slight round cell infiltration. Three specimens in which the lock-stitch method was employed showed epithelial covering of the mucosal defect in one, without gland formation, and a persistent mucosal defect in two. There was much more evidence of inflammation in the line of apposition than in the three layer suture specimens of from six to nine day healing. The silk in two specimens was near the mucosal margin of the anastomosis and was the site of cellular infiltration.

Twenty Day Healing.—Three specimens were studied: two in which the lock-stitch technic was used and one in which the three layer method was employed. The two former specimens showed mucosal regeneration with gland formation, while the latter revealed mucosal union with very little gland formation at the site of operative injury. All the specimens showed a compact fibrous union at the line of apposition and virtually total absence of cellular infiltration. The silk threads in these sections were surrounded by fibroblasts and a hyaline appearing halo, while there was a total absence of leukocytes.

None of these posterior specimens showed mucosal inclusions in the line of apposition.

The foregoing descriptions indicate that in the early stages of healing (six to fourteen days) the three layer method presents more compact union and is complicated by much less inflammation and hemorrhage than the lock-stitch suture. Our data suggest, but do not prove conclusively, that mucosal healing also is probably accomplished earlier in the three layer method. At the end of twenty days there is little histologic difference between the two. In any event the three layer method, on the basis of its excellent early healing, is the preferable one of the two.

In order to make this comparative study more complete, we are now reporting our results with two other posterior suture methods from a third series of animals that so far have not been included in this paper. Other investigators [22] generally voice the opinion that suture of the mucosa is necessary for its rapid healing. In view of the surprisingly good healing obtained anteriorly with suture method 4 (presection), in which no sutures are passed through the mucosa, we decided to try two other posterior methods of suture: one, a two layer posterior method in which the inner catgut suture pierced the entire thickness of the gastro-intestinal wall, except the mucosa, but did not cross or suture the free edge of the mucosa, and the other an ordinary continuous through-and-through suture method similar to anterior method 5. The former method we designated posterior suture method 7; the latter, posterior suture method 5. These sutures are described earlier in the paper, although it should be noted that in posterior method 7, a good bite in the submucosa is necessary if one is to secure even a modicum of hemostasis, and in doing this it is probably inevitable that the intestinal mucosa is pierced occasionally. It should also be noted that when the gastric and intestinal mucosae are sectioned in posterior method 7, they evert, touch and cover the line of suture.

In view of the poor immediate healing with the lock-stitch suture, it seemed interesting to know just how well healing occurred when the posterior ostial suture penetrated all thicknesses of the gastro-intestinal wall as an ordinary continuous suture (posterior method 5).

22. Klose and Rosenbaum-Canné (footnote 9). Strauch (footnote 13).

Posterior Method 7.—Four animals were subjected to this technic and were killed at six, nine, eleven and fourteen days. The healing was remarkable. Six day healing (dog 64) revealed altered glandular mucosa at the site of operative injury, as shown in figure 18. The muscularis mucosae showed only a very narrow defect, while the line of apposition showed a compact granulation tissue with here and there a few aggregations of polymorphonuclear leukocytes. Nine day healing (dog 70) showed the operative site covered with columnar epithelium, while the line of apposition showed less inflammation than in dog 64. Eleven day healing (dog 65) was merely an improvement of that in the nine day specimen. The gastric and intestinal glands were apposed, and there was a conspicuous absence of a broad plateau between gastric and intestinal mucosae. Parietal cells in the gastric mucosa were present within about four gland-widths of the site of gastrointestinal union. A silk suture was present and had an enveloping hyaline zone. Fourteen day healing (dog 71) showed virtually no evidence of inflammation from mucosa to peritoneum, while the gastric and intestinal glands were closely apposed. A silk suture was passing into the intestinal lumen to one side of the line of apposition, and had some intestinal epithelium about it.

Posterior Method 5.—Posterior suture method 5 was used on one animal (dog 72). Nine day healing showed mucosal healing with beginning invagination of the young epithelium for new crypt formation. The line of apposition showed compact granulation tissue with little cellular infiltration. The gastric mucosa at a short distance from the line of apposition showed a rather characteristic change at a point where the stomach wall was pierced by the catgut suture. Here the gastric mucosa had lost its characteristic appearance. The epithelial nuclei and cytoplasm assumed a deeper stain; glands were found; one was rather large and resembled somewhat the marginal cyst on the gastric side of the healed mucosal defect in the same section. Marginal cysts were found in all our posterior suture methods.

The foregoing observations indicate, we believe, that posterior suture methods 5 and 7 are decidedly superior to the lock-stitch suture and also surpass the three layer technic in so far as early healing is concerned.

The complicated healing observed with the lock-stitch method is evidently due to its strangulating effect. This is probably a reasonable inference in view of the rapid and excellent nine day healing obtained with posterior technic 5, which, while it penetrates all coats of stomach and intestine as the lock-stitch does, does not similarly constrict the tissues lying on the ostial aspect of the suture. Obviously, one experiment with posterior method 5 is inadequate and does not warrant the drawing of conclusions.

A comparison of posterior methods 7 and 5 and the three layer technic demonstrates fairly conclusively not only that mucosal suture is unnecessary for early and satisfactory healing but that so-called mucosal suture retards mucosal regeneration. Our findings in this respect corroborate those of Kopyloff, and we can see no logical reason for a posterior three layer suture method. There seems to be little choice between posterior methods 5 and 7, from the standpoint of histo-

logic healing, though technically method 5 is the simpler and more effective for hemostasis. The lock-stitch suture appears most undesirable of all, so far as early uncomplicated healing is concerned. However, it must be admitted that so far as remote healing is concerned, all four methods apparently give the same ultimate result.

Continuous Silk Sutures.—Our observations in this study indicate that, as a general rule, there is a tendency for the posterior continuous serosubmucosal silk suture to migrate toward the gastro-intestinal lumen and to be associated with varying degrees of inflammatory reaction. There are exceptions to this, for in some sections no silk was seen, while in others the silk showed neither evidence of surrounding inflammatory reaction nor a tendency to migrate toward the mucosa.

Actual penetration of the intestinal mucosa by a silk suture was observed only once (dog 71) and indicates that even here, where the suture is placed before any distortion makes its accurate placement difficult, the intestinal lumen may be pierced inadvertently and lead to epithelial inclusions in the intestinal wall. No appositional rests were observed in any of the sections from the posterior aspects of the gastro-intestinal ostia, and this would substantiate our observations on anterior ostial healing, that mere penetration of the entire thickness of stomach and intestinal wall by plain 00 catgut is not a factor in the production of mucosal inclusions in the line of apposition.

SUMMARY AND CONCLUSIONS

This study is based altogether on experimental observations on forty-four dogs. Anterior gastroduodenostomies were performed by various suture methods, while the suture material was uniform throughout.

A group of five dogs from another series was utilized in this report to give a more complete comparison of healing on the posterior aspect of the gastroduodenal ostium.

The purpose of this study was to determine whether serosal cysts would form between apposed peritoneal surfaces and also what differences, if any, occurred in healing following the use of various suture methods.

Our most rapid and uncomplicated healing on the anterior aspect of the gastroduodenal ostium was obtained by the use of a single layer of serosubmucosal presection silk sutures (Halsted), which were termed suture method 4. This observation indicates, we believe, that separate suture of the mucosa (mucosa and submucosa), whether employed anteriorly or posteriorly as in the three layer suture methods, not only is unnecessary for rapid mucosal healing, but is probably a retarding factor and therefore an undesirable as well as an added technical step.

It also emphasizes the adequacy and desirability of the single layer suture method of Halsted, when applicable.

Our next most rapid anterior healing occurred with suture methods 1 (Connell), 3 (baseball stitch) and 6 (three tier). From the single standpoint of firm union along the line of apposition they offer not much difference, while suture method 5 (ordinary continuous suture) in some of the early healing preparations showed most profound inflammatory changes.

Mucosal healing, like healing along the line of apposition, was most rapid with method 4 (one layer presection sutures). Next in order of rapidity is method 3, followed by methods 6, 5 and 1, with probably little choice between the latter three on this particular point.

Our observations indicate that mucosal inclusions develop in the intestinal wall when the mucosa is pierced by a silk suture. This observation, originally made by Mall, has been confirmed by Flint. Other observers have noted these inclusions, but apparently do not recognize their etiology or possible significance.

Sutures placed on the anterior aspect of the gastroduodenal ostium so as to evert the mucosa often cause the displaced epithelium to develop in the line of gastroduodenal apposition, as a persistent adenomatous structure of varying size. The two suture methods (technics 3 and 5) generally advised by English surgical textbooks possess this unrecognized, undesirable and easily avoidable technical fault; it is therefore questionable whether the recommendation of some authors to use suture methods that evert gastro-intestinal mucosa for purposes of hemostasis is sound advice.

Four types of suture methods were used on the posterior aspect of the gastroduodenal ostium. Our best healing was obtained either with an inner row suture passed through all coats of stomach and intestine as an ordinary continuous stitch or with a similar suture passed through serosa and submucosa leaving the cut edges of the mucosa free. The latter confirms our observations on the anterior aspect of the ostium, that separate suture of the mucosa is not necessary for rapid mucosal healing. Next best posterior healing was obtained with the three layer suture technic, and most undesirable of all was the healing following the use of an inner row lock-stitch suture, which we believe has a strangulating effect on the involved tissue.

It is therefore evident that there is a distinct difference in healing following gastroduodenal anastomosis depending on the suture method employed. However, in all fairness to the Connell stitch anteriorly and the lock stitch posteriorly, we admit that no untoward complications developed from their use, and firm healing eventually occurred.

We believe that our observations warrant the conclusion that fine plain catgut, when passed through the entire thickness of stomach or

intestinal wall, does not cause the development of mucosal inclusions along the course of the suture, as in the case of improperly placed silk suture material. However, through-and-through catgut sutures as used by us on the anterior aspect of the gastroduodenal ostium produces decidedly more inflammatory reaction in the healing process than methods in which they are not used; this is particularly true of the Connell suture, which probably acts as a strangulating agent.

Our observations also indicate that when silk suture material is placed without piercing the gastro-intestinal lumen, its presence causes practically no inflammatory reaction. Halsted sutures so placed tend to migrate toward the serosa, while those that pierce the mucosa become infected, are the cause of mucosal inclusions in the intestinal wall and slough into the lumen either through the intestinal wall or along the line of apposition.

If silk suture material is used, it is probably preferable to use interrupted sutures. While our observations are not conclusive, they are most suggestive that continuous silk serosubmucosal sutures show a definite tendency to migrate toward the mucosa. The reason for this is probably that if the continuous suture penetrates the mucosa at any one point, the entire suture may serve as a track along which the inevitable infection may spread. We therefore consider the continuous silk suture as undesirable for gastro-intestinal anastomosis.

Nothing that could be interpreted as a serosal inclusion was observed in this study, and the conclusion is probably justified that serosal inclusions, if they do form, are at best rare occurrences in which serosal surfaces unite under an inflammatory stimulus.

No experiments were done in which so-called redundant mucosa was excised prior to suture of the anterior aspect of the gastroduodenal ostium. We believe that our observations suggest the inadvisability of such a procedure, although it is one still commonly practiced, since none of our specimens showed overlapping of gastric and intestinal mucosa at the line of anastomosis. In fact, with some suture methods well marked mucosal defects occur which would probably be considerably enlarged by the excision of additional mucosa.

Dr. William F. Allen provided assistance from the department of anatomy in preparing our histologic material. Miss Clarice Ashworth made the drawings, and Mr. Walter Johnson the photomicrographs.

ETIOLOGY OF GALLSTONES

IV. IS CHOLESTEROL EXCRETED BY THE GALLBLADDER MUCOSA?

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Ever since the early investigations of Naunyn [1] and his associates,[2] the problem of an excretion of cholesterol and calcium by the gallbladder has remained unsettled in spite of considerable literature on the subject. Since many of these studies were made, the ideas of cholesterol metabolism have undergone such radical changes that a restatement of a few basic facts is important.

To begin with, when cholesterol is mentioned, one is apt to think at once of the liver and bile as the important organ in its metabolism. This is totally unwarranted in the light of modern knowledge. In man, the blood contains about twice as much cholesterol as the bile. According to the work of Sperry [3] and others,[4] reviewed in a previous paper, the overwhelming proportion of the cholesterol excreted is excreted in the intestinal mucosa, this being a far more important route than the biliary. In the dog, the commonest experimental animal used in studies of gallstones, the discrepancy is still more marked. The blood of the dog has a much higher cholesterol content than that of man; the

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2. Thomas: Ueber Abhängigkeit der Absonderung und Zusammensetzung der Galle von der Nahrung, Diss., Strassburg, 1890. Kansch: Ueber den Gehalt der Leber an Galle und Cholesterin, Diss., Strassburg, 1891. Jankau, L.: Ueber Cholesterin und Kalkausscheidung mit der Galle, Arch. f. exper. Path. u. Pharmakol. **19**:237, 1891.

3. Sperry, W. M.: Lipoid Excretion: IV. A Study of the Relationship of Bile to the Fecal Lipoids with Special Reference to Certain Problems of Sterol Metabolism, J. Biol. Chem. **182**:351, 1926-1927.

4. Buerger, M., and Oeter, H. D.: Ueber den Cholesteringehalt der menschlichen Darmwand, Ztschr. f. physiol. Chem. **182**:141, 1929. Beumer, H., and Hepner, F.: Ueber die Ausscheidungswege des Cholesterins, Ztschr. f. d. ges. exper. Med. **64**:797, 1929.

normal level is from 200 to 300 mg. per hundred cubic centimeters. This is in marked contrast with the exceedingly low figures found for the hepatic bile of the dog, in which from 10 to 20 mg. per hundred cubic centimeters is the average.

Next is the fact, first mentioned by Rous and McMaster,[5] that the biliary tract is exceedingly sensitive to infection if a fistula is established. They were able to keep the bile in their dogs sterile only by inserting a very long tube, which was allowed to coil up in the abdomen before it was led to the surface. If this precaution was neglected, the bile soon became infected and had a heavy sediment. We called attention in a previous paper [6] to the fact that if stasis occurs in the biliary tract of a dog, especially if the cystic duct is ligated, a prompt endogenous infection of the bile occurs. Pus cells and bacteria can be found in abundance in the bile, and microscopic examination reveals infection of the gallbladder, especially on its hepatic surfaces. This work makes it obvious that in most experimental procedures on gallbladders of dogs one has the element of infection to consider.

Naunyn early called attention to the fact that pus contained a high percentage of cholesterol. This content averages about 300 mg. per hundred cubic centimeters, and in many specimens, as high as 500 mg. per hundred cubic centimeters. It is obvious, therefore, that even a minimal infection raises the cholesterol content of the bile of dogs to many times its normal content.

With these points in view, we shall consider but a single one of the recent publications on the subject of secretion of cholesterol into the gallbladder, that of Elman and Graham.[7] These authors found that the gallbladder added cholesterol to the bile in considerable amounts, which they could not account for in any way except as a secretion of its mucosa. The specimens were secured by aspiration of the gallbladder through the liver substance so as to prevent leakage of bile. A short calculation shows that if but a few drops of blood or serum leaked through the needle hole into the gallbladder, these would account for even the highest rise reported, 300 per cent. This does not take into consideration the possibility of increase of the cholesterol content from leukocytes, which disintegrate rather rapidly in bile.

The problem of the solution of cholesterol-containing débris by bile is a difficult one to answer until it is discovered how it is held in

5. Rous, P., and McMaster, P. D.: A Method for the Permanent Sterile Drainage of Intraabdominal Ducts as Applied to the Common Duct, J.Exper.Med. **37**:11, 1923.

6. Andrews, E., and Hrdina, L.: Hepatogenous Cholecystitis, Arch. Surg. **23**:201 (Aug.) 1931.

7. Elman, R., and Graham, E. A.: The Pathogenesis of "Strawberry" Gallbladder, Arch. Surg. **24**:14 (Jan.) 1932.

solution in the blood. Cholesterol is insoluble in blood serum in vitro, and it is probably held in some chemical compound with the proteins. As to the bile, cholesterol is very slightly soluble in solutions of bile salts, not nearly to the amounts of the normal content of human bile. It has been shown by us in a previous paper [8] that it is not simply dissolved, but is held in a definite chemical compound with the various bile acids that have the power to make it soluble in very high concentrations in an additional compound, the isolation and also the synthetic preparation of which was described. In experimental work on dogs it is exceedingly difficult to tell if the cholesterol in infected bile is really in solution or not, as it may be present in such a very fine amorphous state that it passes rapidly through filter paper, leaving cloudy filtrates even after the leukocytes have been removed.

Our own experiences bearing on this subject have been from the analysis of the content of hydropic gallbladders whether with or without calcium carbonate stones. The results have been as follows:

1. In all clinical cases of long-standing obstruction of the cystic duct in which all the bile salts and pigment have been absorbed, there has been absolutely no cholesterol held in solution; it was all in the form of a crystalline emulsion. It seems, therefore, that there is no substance other than bile salts in the bile capable of holding the cholesterol in solution. This speaks against the origin of gallbladder cholesterol from the body fluids, where it is probably held in solution in some other matter. Although obviously some such material must pass into the gallbladder, its solubility in the other substance enables it to be reabsorbed.

2. Although the amount of cholesterol in the contents from hydropic gallbladders is often much higher than is found in normal bile (up to 600 mg. per hundred cubic centimeters), it has never been our experience to find a greater total in the gallbladder than one would theoretically expect to get from the precipitation of the normal amount of cholesterol from the average human gallbladder (volume from 35 to 40 cc.).

If the bile acids have all been absorbed as they usually have in long-standing hydrops, the cholesterol is always in the form of an emulsion and none is in solution. If cholesterol were excreted in the gallbladder, one would naturally expect to find a far larger amount than that theoretically expected to be derived from the bile in the gallbladder at the time the obstruction of the cystic duct took place. Graham's figures on the cholesterol content of the hydropic gallbladder show a cholesterol content actually below that to be expected, and hence in our opinion do not indicate any excretion by the gallbladder mucosa.

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8. Andrews, E.; Schoenheimer, R., and Hrdina, L.: Studies on the Etiology of Gallstones: I. Chemical Factors and the Rôle of the Gallbladder, Arch. Surg. **25**:796 (Oct.) 1932.

3. The cholesterol is almost uniformly crystalline in form, indicating that it has come from the bile and not from the débris of cells, when it would naturally be in the amorphous form. This statement cannot be considered as final, as it is impossible to tell in a smear whether one is seeing cholesterol in amorphous form or the calcium carbonate, which may greatly exceed it in amount. One can positively state, however, that the débris always contains cholesterol crystals.

In a recent communication, Phemister and his co-workers [9] showed that if the human cystic duct is obstructed for long periods, there is an excretion into the gallbladder of large amounts of calcium. This is in the form of a white, creamy emulsion of almost pure calcium carbonate. Furthermore, if cholesterol stones are already present, obstruction of the cystic duct will bring about a deposit of calcium on the periphery of such stones. This study is quite conclusive and is supported by a series of clinical cases and roentgenograms, as well as by stones removed at operation, with analyses of the gallbladder contents. The important point in relation to our studies is that in no case was there present in such gallbladders any increased amount of cholesterol. Of seven gallbladders reported on by Phemister, one contained a trace of cholesterol and the others none.

Experimental studies on this subject, as we have noted in an earlier paragraph, are beset with almost insuperable difficulties. The possible errors from infection in the gallbladder or from the pouring of a little serum or blood are, as we have said, far greater than the expected experimental variations. Light may, however, be thrown on the problem by certain means.

In the first place, experiments with ligature of the common duct are important. If the common duct is ligated, bile will distend the gallbladder, and after it is once filled, will lie there with little further addition from the liver. Its concentration soon reaches a maximum (about 25 per cent total solids), following which there is very slow further absorption of water. Further concentration is a matter of months, not days. Under such conditions, if secretion of cholesterol by the wall of the gallbladder takes place, one would expect that a gradual mounting in the cholesterol content would take place. Added to this is the possibility of infection under these circumstances, which would increase the cholesterol. Graham reported a series of three experiments in which stasic bile showed a marked increase in cholesterol content. This was probably due to leakage of serum or to infection about the needle holes, as we have done a series of forty-two such experi-

9. Phemister, D. B.; Rewbridge, A. G., and Rudisill, H., Jr.: Calcium Carbonate Gall Stones and Calcification of the Gallbladder Following Cystic Duct Obstruction, Ann. Surg. **94**:493, 1931.

ments, omitting the needle puncture and using thirty-seven normal dogs as controls, and as may be seen from the accompanying table, the results are diametrically opposed to Graham's. A study of this long series has not revealed the slightest increase in the bile cholesterol. It varies between 30 and 100 mg. per hundred cubic centimeters, averaging about 50 mg. per hundred cubic centimeters, and in dogs with prolonged obstruction of the common duct it is not only no higher, but on the average slightly lower, being, however, within the limits of experimental error.

Bile from the gallbladders in six human cases of jaundice also were studied, and the figures fell within the normal range of human values.

Attempts were made to study the normal secretion of the isolated gallbladder, most of which were failures. As previously reported by us,[6] if the dog's cystic duct is ligated and the bile washed out and the hole closed, the result will be the prompt onset of a violent sepsis. The viscus will often be filled with a purulent secretion, which of course contains a high sterol content, as does any other pus. Another series

Cholesterol Content of Gallbladder Bile in Stasis

	Av. Content, Mg. per 100 Cc.
Controls: 36 dogs with stasis of 24 hours or less	57
42 dogs with ligature of common duct, 3-58 days	51

was studied as follows. The gallbladder was isolated by ligature of the cystic duct and brought up to the skin and a drain inserted. The fistula thus produced, for several weeks secreted a purulent material with a high cholesterol content. This secretion gradually became clearer, and the cholesterol content was much less. Finally the drain was removed, and the wound was allowed to heal. After several openings and closings, it finally stayed closed. After several months the animals were put to death; the gallbladders were removed and the contents studied. In several, it was found that the duct had reopened and the gallbladder was full of bile. In several others, the organ was still infected and contained frank pus. Only one experiment had been entirely successful. Dog 268 was operated on on June 3, 1931, drained for about two weeks and was put to death Jan. 12, 1932. In this dog, the findings were remarkably like those reported by Phemister in human beings. The contents of the gallbladder were pure white and consisted of a creamy, viscid, opaque material. The walls were thickened and whitish gray. Microscopic examination showed that no pus cells were present and very few mononuclear cells (about one or two per field). Chemical analysis showed that the gallbladder contents contained but 21 mg. of cholesterol per hundred cubic centimeters and 580 mg. of

calcium per hundred cubic centimeters. This was the only case in our entire series in which it had been possible to get a clean, pus-free secretion from the gallbladder of the dog, and while it is rash to generalize from the result of a single experiment, we believe that it offers some further proof that the excretion of the mucosa of the normal gallbladder is rich in calcium and poor in cholesterol.

Another almost exactly similar observation was made in a clinical case, no. 41658. A woman, 76 years old, had undergone a cholecystostomy twenty-two years before; no bile had drained, but only mucus for several weeks, following which the wound closed and remained so until just before admission when a fistula of the gallbladder was presented. This drained no bile, and the patient was perfectly normal except for the discharge. This was of a double character, being composed mostly of a clear, watery fluid evidently from the gallbladder itself, but also containing an occasional gush of pus from the granulating tract. This interpretation was confirmed at operation in which the tract was excised and a cholecystectomy was done. Chemical studies of the discharge from this fistula showed that the purulent portion of it contained a high percentage of cholesterol, 510 mg. per hundred cubic centimeters. The clear part, however, contained only the faintest trace of cholesterol (less than 1 mg. per hundred cubic centimeters). This offers another confirmation of the fact that the clean secretion of the gallbladder does not take part in the formation of cholesterol stones.

COMMENT

In a previous paper [10] it was shown that infection of a dog's gallbladder caused a marked fall in the calcium content of the stagnant bile.

In the control series, in which it appears that slight infection must have taken place, the fall in the calcium was much less, about 20 per cent as against about 60 per cent in the violently infected ones. These findings are in marked contrast to the secretion of calcium found in the human cases by Phemister and the single successful experiment on a dog reported in a previous paragraph. The explanation probably lies in the reaction of the bile, or more strictly, of the contents of the gallbladder, which in the latter group are generally free from bile salts and pigment. In our earlier experiments there must almost certainly have been a marked fall in the p_H value and acidification of the bile. Rous showed that the bile of the gallbladder underwent marked acidification in the process of concentration in dogs. This, of course, would increase the solubility of the calcium and favor absorption. The exact opposite was shown to be the case by Phemister,[9] who found quite high p_H values in his cases of calcium carbonate milk in the gallbladder. In

10. Andrews, E., and Hrdina, L.: Absorption of Calcium from the Gall Bladder, Am. J. M. Sc. **181**:478, 1931.

our single successful experiment on a dog there was not sufficient material to make this determination. However, alkalinity tends to reduce the solubility of calcium and would not favor its absorption.

The problem, then, appears to be answered as follows: In the normal concentrating action of the gallbladder, the calcium is concentrated to about the same extent as the other ingredients of the bile. This was shown by us quite clearly in a former paper.[8] During this process, as Drury [11] and his co-workers showed, marked acidification takes place. This acidification is accentuated by the presence of infection, which is likely to occur in any static bile, and by this means the absorption of calcium is hastened. If however, the cystic duct is closed over very long periods, the bile is absorbed and the tendency to infection overcome. Then the tissue fluids secreted into the gallbladder are unusually alkaline, and calcium is precipitated and accumulated in the form of pure calcium carbonate, the more soluble salts being resorbed.

In the case of cholesterol, the exact opposite is the case. The infection accompanying stasis brings about the excretion of migrating cells containing large amounts of cholesterol as well as serum, which in most animals is richer in cholesterol than even the concentrated bile of the gallbladder. This cholesterol is not in soluble form and cannot be laid down in the crystalline gallstones. This phase of the problem has often been lightly dismissed, but it is impossible to explain chemically the changing of an amorphus débris into a crystalline gallstone. The existence of large crystals implies that cholesterol crystallized out of solution.

If the ducts are open, the slight amount of mucosal secretion will be washed out. If they remain closed, either an abscess develops or sterilization occurs, after which the findings of very low cholesterol values is the usual one. In any event the cholesterol excreted by the mucosa takes no part in the formation of gallstones.

CONCLUSIONS

1. Cholesterol, although excreted by the infected gallbladder, is not excreted in appreciable amounts by the mucosa of the normal gallbladder.

2. The mucosa of the gallbladder takes no part in the formation of cholesterol stones.

3. Calcium is excreted in large amounts by the mucosa of the normal gallbladder, and this is an important factor in the building of gallstones.

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11. Drury, D. R.; McMaster, P. D., and Rous, P.: Observations on Some Causes of Gall Stone Formation: III. The Relation of the Reaction of the Bile to Experimental Cholelithiasis, J. Exper. Med. **39**:403, 1924.

CALCINOSIS UNIVERSALIS

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The purpose of this paper is to present a case of a rare condition and a treatment which yielded satisfactory results. The case was observed at frequent intervals for a period of four years.

Since there is considerable similarity between calcinosis universalis and progressive myositis ossificans, there was difficulty in identifying the condition presented by my patient. Because of the presence of true subcutaneous calcareous deposits along the fascial planes and a lack of ossification and involvement of the muscles, the case was considered one of calcinosis universalis.

Calcium deposits have been found previously in many organs and tissues in various conditions, the calcification quite frequently being an end-result of a degenerative process. Generalized calcium deposition of an unknown cause was first described by Verse.[1] Since then other cases have been added to the literature. Not infrequently, associated with calcinosis universalis were other conditions, such as scleroderma, dermatomyositis and myositis fibrosa. Langmead [2] expressed the belief that the cause underlying these four disorders is probably the same.

Various theories were advanced as the cause of calcinosis universalis. Craig and Lyall [3] expressed the belief that it is a disturbance of the calcium-phosphorus balance. A parathyroid dysfunction was advanced as the cause, and parathyroid extract was suggested for treatment. In a child of 3½ years Morse [4] found that the calcification was preceded by a degeneration of fat. Virchow described a condition which he labeled metastatic calcification. Wells,[5] Schulze [6] and others showed that the condition studied by Virchow presents an oversaturation of the blood with calcium salts, and the calcium deposition occurs without a previous

1. Verse, M.: Ueber Calcinosis universalis, Beitr. z. path. Anat. u. z. allg. Path. **53**:212, 1912.

2. Langmead, F. S.: Relationship Between Certain Rare Diseases: Scleroderma, Calcinosis, Dermatomyositis, Myositis Fibrosa, Arch. Pediat. **40**:112, 1923.

3. Craig, John, and Lyall, Alexander: A Case of Calcinosis Universalis, and a Suggested Method of Treatment, Brit. J. Child. Dis. **28**:29, 1931.

4. Morse, John Lovett: Calcification of the Skin in a Child, Am. J. Dis. Child. **22**:412 (Oct.) 1921.

5. Wells, H. G.: Metastatic Calcification, Arch. Int. Med. **15**:574 (April) 1915; Tr. Chicago Path. Soc. **9**:208, 1914-1915.

6. Schulze, F.: Skelettveränderungen als Ursache von Verkalkungen, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **36**:243, 1923.

degeneration of tissue. Wells also pointed out that the calcium is deposited in areas in which carbon dioxide is least abundant.

Tisdall and Erb [7] reported two cases of calcium deposition in the skin with normal blood calcium and phosphorus. They expressed the belief that some local condition was the determining factor in the deposition of calcium. Bauer, Marble and Bennett,[8] studying the case of Wilens and Derby,[9] did not find fatty degeneration, inflammation or tissue necrosis. The blood calcium of the patient was normal, and they believed that the calcium deposition was due to an abnormal calcium and phosphorus metabolism.

It is generally agreed that the treatment of calcinosis universalis is futile and the condition is progressive. Craig and Lyall [3] reported a case in which the calcium disappeared in sixty days following the administration of disodium phosphate. Kennedy [10] advised a ketogenic diet. Frolich [11] treated a patient with progressive myositis ossificans with a high fat diet. He believed that calcium deposition could be prevented by such a diet, basing his view on the gradual disappearance of some of the calcium and an absence of new deposits in his patient.

REPORT OF A CASE

History.—A girl, aged 6½ years, was first seen on Feb. 4, 1928. She had difficulty in walking because of contraction of both Achilles tendons and a resulting equinus. She walked on the forepart of her feet. She had painful and indurated areas on her extremities. She had had measles at 3 years, "intestinal flu" at 4, whooping cough at 5, tonsillectomy at 5, chickenpox at 6 years and pneumonia three times between the ages of 3 and 5. Her present difficulty began four years prior to examination when she began to fall down. Two and a half years later her joints became "stiff."

Examination.—At the time of the first examination she had a temperature of 100 F. and a pulse rate of 90. The conjunctivae were slightly injected, and the veins of the eyelids were dilated. There was induration of both pectoralis major muscles as they bridged the axillary space. The inguinal glands were enlarged. There were also indurated masses in both biceps tendons, and the elbows could not be extended beyond 80 degrees. The shoulder joints were normal. The forearms, the hands and the fingers were normal. There were similar indurated masses in both hips, but with no limitation of motion. The thighs were indurated, the con-

7. Tisdall, F. F., and Erb, I. H.: Report of Two Cases with Unusual Calcareous Deposits, Am. J. Dis. Child. **27**:28 (Jan.) 1924.

8. Bauer, W.; Marble, A., and Bennett, G. A.: Further Studies in a Case of Calcification of Subcutaneous Tissue ("Calcinosis Universalis") in a Child, Am. J. M. Sc. **182**:237, 1931.

9. Wilens, Gustav, and Derby, Joseph: Calcification of Subcutaneous Tissue in a Child (Calcinosis Universalis), Am. J. Dis. Child. **31**:34 (Jan.) 1926.

10. Kennedy, R. L. J.: Calcinosis and Scleroderma in a Child Treated by Ketogenic Diet, M. Clin. North America **12**:1655, 1929.

11. Frolich, Theodor: La myosite, ossificante progressive, traitée par le jeune hydrocarbone (l'acidose artificielle), Acta pædiat. **5**:294, 1926.

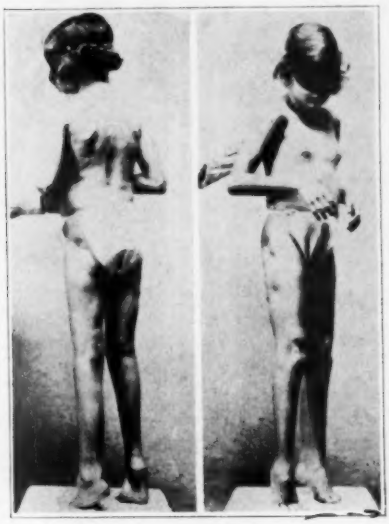

Fig. 1.—Photographs taken after four years of observation. Note the scars on the right thigh and on the right and left buttocks, where calcareous areas broke down; also note the position of the feet.

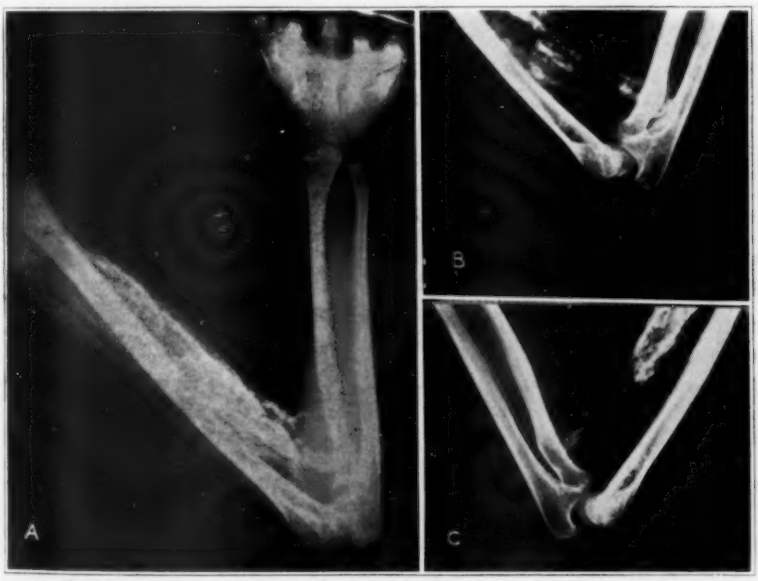

Fig. 2.—Roentgenograms taken at the first examination, in February, 1928. Note the involvement of the biceps muscle in *A*, and also the manner in which the biceps tendons are involved in both elbows (*B* and *C*).

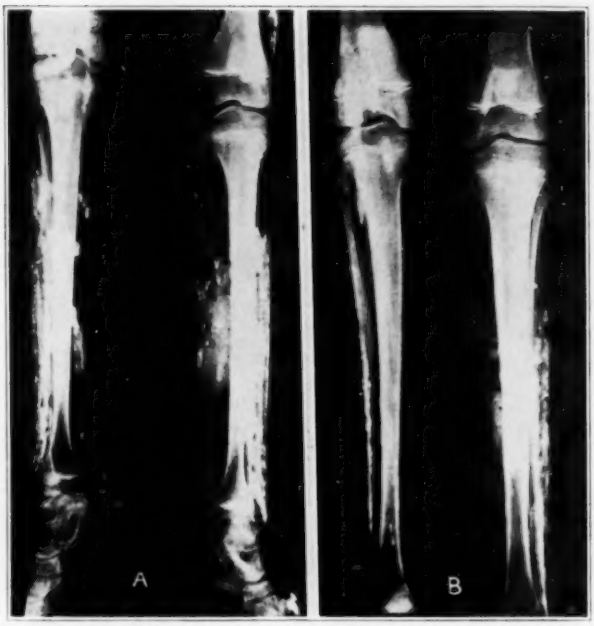

Fig. 3.—*A*, roentgenogram taken in February, 1928. Note the involvement of the extensor tendons to the dorsum of the foot. *B*, roentgenogram taken in October, 1931. Note the marked disappearance of the calcium deposit as contrasted with *A*, taken three years previously.

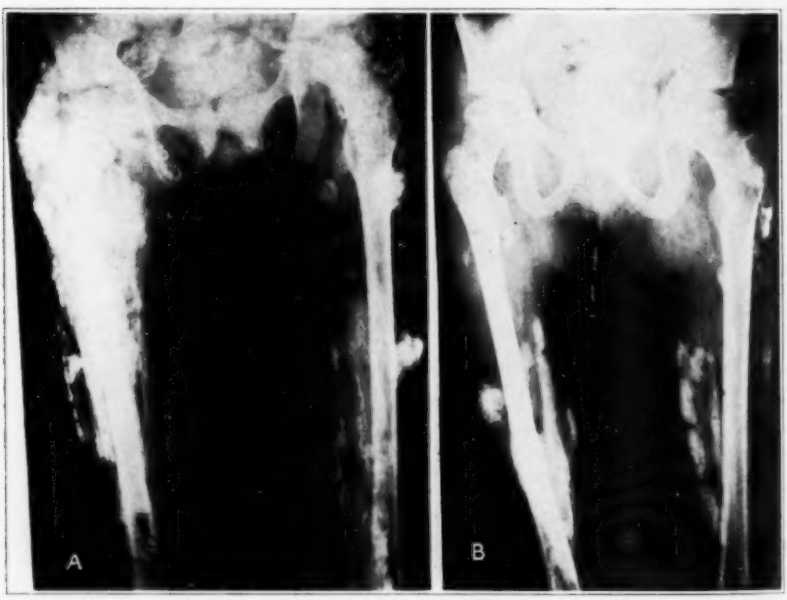

Fig. 4.—*A*, roentgenogram taken in February, 1928. *B*, roentgenogram taken in October, 1931. Note the diminished amount of calcium about the buttocks and thighs as contrasted with the roentgenogram taken three years previously.

dition being more pronounced on the left side. There was contraction of both Achilles tendons with induration of the left one. The right ankle joint was fixed, but there was some motion in the forepart of the right foot. The left ankle joint had a marked limitation of motion. The indurated areas began as small, red, painful, subcutaneous nodules, enlarging progressively and diffusing into the surrounding tissue. The older areas were painless. Often two or more of these nodules coalesced; some of them had a soft center, broke through the skin and discharged calcareous material.

At the first examination, roentgenograms were taken of the entire osseous system. There were marked calcareous deposits along the fascial planes in both

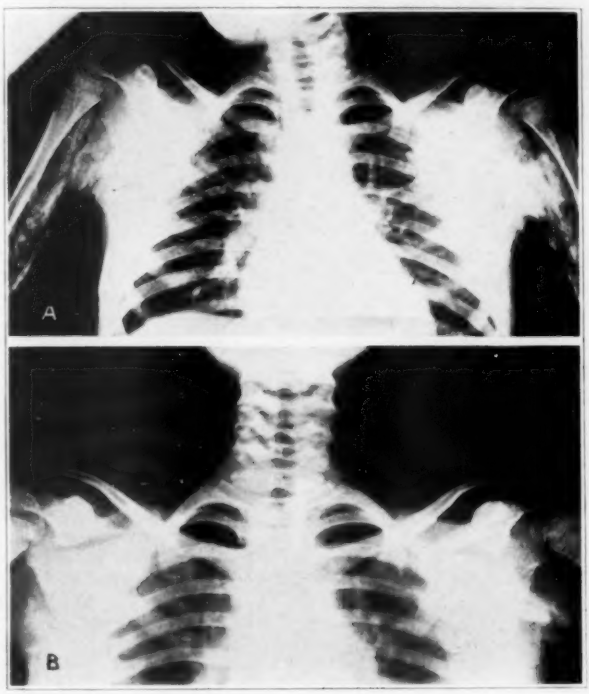

Fig. 5.—*A*, roentgenogram taken in February, 1928. Note the calcareous deposits about the axillae. *B*, roentgenogram taken in October, 1931. Note the marked disappearance of the calcium deposits.

gluteal regions, the thighs, most marked on the left, about both knee joints, the popliteal space, the calves of both legs and along the extensor tendons of the feet. There were also deposits in the pectoralis major muscles and in the upper and posterior parts of the arms, as well as involvement of the biceps tendons.

The white blood count was 7,600, with 68 per cent polymorphonuclears, 32 per cent lymphocytes and 80 per cent hemoglobin; the red blood count was 4,200,000. The reactions to the Wassermann and Pirquet tests were negative. The blood calcium was 16 mg. on Feb. 11, 1928; 11 mg. on May 26, 1928; 10 mg. on Aug. 20, 1930, and 10.8 mg. on Jan. 19, 1932.

A nodule was removed in February, 1928, from the right thigh. The nodule was intimately attached to the fascia lata. Grossly, the tissue was grayish white with small firm granules. Microscopically, the tissue showed a marked infiltration of calcium arranged in globules of varying sizes. The connective tissue was swollen, edematous and, in places, necrotic. There was an occasional giant cell containing calcium granules.

Fig. 6.—Section of a nodule removed from the external aspect of the right thigh in February, 1928. *A* shows deposition of calcium. *B* shows edema and swelling of the tissue, with necrosis in some areas. The entire right edge contains calcium in rather circumscribed nodules of varying sizes. There is an occasional giant cell. There are no bone cells.

Treatment.—The mother noticed a marked improvement in the patient during the summer months, when the child played in the sunshine, and a progression of the disease during the winter months. Because of this observation a course of heliotherapy was outlined. The exposures were gradually increased to cover the entire body daily. The first exposure was for five minutes, which was gradually increased to three or four hours daily. The mercury quartz light was used during the months of the year in which sunshine was not available. This treatment was

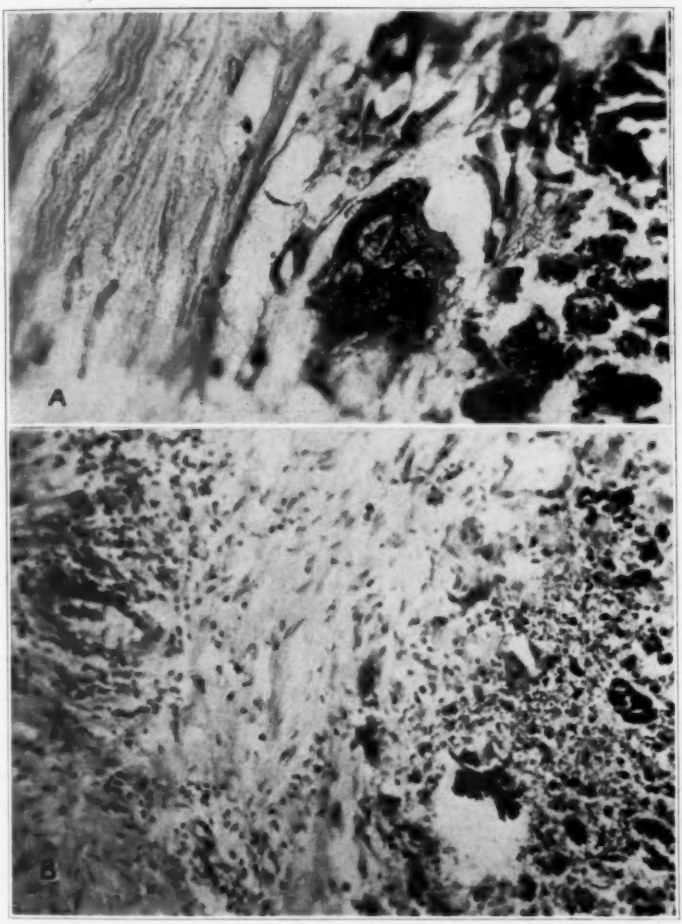

Fig. 7.—Sections removed in October, 1931, three years after the first biopsy. *A* shows numerous giant cells filled with small particles of calcium. The calcium is in small granules instead of large deposits, as seen in figure 6. The connective tissue shows absence of swelling and only slight edema. *B* shows a mononuclear infiltration, giant cells and a granular deposit of calcium.

administered during the four year observation period. No other treatment was given during this time. During the fall, winter and spring of 1929 and 1930, the patient resided in Arizona. After eight weeks of the treatment the blood calcium

fell from 16 to 11 mg. No new painful indurated areas were found. The old areas became painless. The temperature did not rise above 99 F., and the headaches disappeared. Several indurated areas broke down but healed promptly. The roentgenograms taken at six month intervals over four years showed a gradual disappearance of the calcium. A biopsy done in October, 1931, showed numerous giant cells filled with granules of calcium. The calcium deposits consisted of minute granules instead of large masses as in the previous biopsy material. The connective tissue did not show necrosis and swelling and only a slight edema. There was a moderate mononuclear infiltration. It was apparent that the method of removal of calcium was by means of a foreign body giant cell reaction with some unknown factor producing granularity of the large masses of calcium.

SUMMARY

A case of a diffuse calcium deposition in fascias (calcinosis universalis) is presented. Heliotherapy apparently produced a gradual disappearance of the calcium as observed by progressive roentgenograms. There was associated a definite clinical improvement. The removal of the calcium apparently was accomplished by a giant cell reaction preceded by a fine granularity of the large masses of calcium.

Dr. Bernhard Steinberg, Director of Laboratories and Research of Toledo Hospital, assisted me in the pathologic descriptions and the photographs.

316 Michigan Street.

TRAUMATIC ENCEPHALITIS

CASE REPORTS OF SO-CALLED CEREBRAL CONCUSSION WITH ENCEPHALOGRAPHIC FINDINGS

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AND
HOWARD B. HUNT, M.D.
OMAHA

The increasing number of cases of trauma of the head presents a problem of major importance to all branches of the medical profession. From automobile accidents alone there were 31,000 deaths in 1931 in the United States, and the total number of accidents for the year extended into the millions. Injuries of the head are frequent among such accidents.

There has been a marked therapeutic advance in the management of the severer types of acute injuries of the head in the past decade, owing to the increasing general knowledge of the diagnosis and treatment of cerebral edema and hemorrhage. Also, the surgical indications are fairly well agreed on by all authorities.

The milder degrees of cerebral trauma, which at the time of the accident are usually called cerebral concussion, representing types of injury to the brain without acutely increased intracranial pressure, with or without fracture of the skull, have not in our opinion received the study they deserve. In the past the results of treatment of this group of patients, in which there is a large number, have been unsatisfactory. A large percentage of the patients have residual complaints, and the question as to whether their complaints were on a psychogenic or an organic basis has not been clear.

Some of the patients show diffuse neurologic signs, mental symptoms, personality changes, palsies of the cranial nerves and bilateral findings, but no focal signs. These findings are not entirely attributable to cerebral edema, but are probably the result of multiple punctate hemorrhages throughout the brain tissue. This condition is a true type of traumatic encephalitis, and in some cases additional subarachnoid hemorrhage is present.

A much larger group of patients, however, who suffered from so-called concussion, never showed any organic signs of neurologic

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structural disease. The acute concussion was presumed to be an essentially transient state not producing structural damage to the nervous system. Nevertheless, the patients continued to complain for long periods of numerous symptoms, such as headache, vertigo, tinnitus, disturbance of sleep and inability to concentrate.

Glaser and Shafer,[1] in a study of 255 cases of trauma of the head, found 140 cases, or 54.9 per cent, without fracture of the skull. They found organic neurologic signs in only 18.5 per cent of these cases. Yet 90 per cent of the group of patients had profound subjective complaints. The studies showed that chronic headaches persisted more often in the group without fracture of the skull than in the group with fracture of the skull. Also, the older the patient, the more likely he was to have prolonged complaints. Unfortunately, their studies were not confirmed by encephalographic examinations.

Pommé and Liégeois [2] reported persistent subjective symptoms in 113 soldiers who sustained wounds of the head during the World War. The patients all had either fracture of the skull or cerebral concussion.

Because of the absence of objective findings on neurologic examination, the conditions in the patients studied were usually diagnosed as posttraumatic psychoneuroses. More recent diagnostic studies of these patients by careful observers have usually shown a characteristic and demonstrable cerebral disorder that exists even without definite neurologic findings. Many of the patients showed reactions similar to those seen following acute epidemic encephalitis.

By the method of encephalography we are able to visualize accurately and to determine the amount of structural damage to the intracranial contents. The more common findings shown by encephalographic studies are extensive cortical or cerebral atrophy, hydrocephalus (external and internal) and arachnoiditis, with obstruction to various cerebrospinal fluid pathways.

The general medical profession is still slow to recognize the tremendous advance in intracranial diagnoses brought about as a result of cerebral visualization by this method. This procedure should be in more general use, as it removes much of the guesswork in clinical neurology. The procedure should be recommended in all cases of cerebral injury in which there is a question of diagnosis. It is of extreme value in certain medicolegal cases in which the question of the

1. Glaser, M. A., and Shafer, F. P.: Skull and Brain Traumas: Their Sequelae; A Clinical Review of Two Hundred and Fifty-Five Cases, J. A. M. A. **98**:271 (Jan. 23) 1932.

2. Pommé, B., and Liégeois, R.: On the Subjective Syndrome Common to Head Injury, Rev. neurol. **1**:483 (April) 1931; quoted in Neurology, Practical Medicine Series, Chicago, Year Book Publishers, Inc., 1931, p. 60.

extent of cerebral damage is present. It gives accurate diagnostic information not obtainable in any other way. It should also be recommended from a therapeutic standpoint. Frazier, Penfield, Fay and others who have made large numbers of encephalograms reported that a percentage of their patients are relieved of severe posttraumatic symptoms.

The pathologic causes of the profound changes seen on encephalography, particularly in cortical atrophy, are in dispute. There are probably several factors, one or more being operative in each case. Fay [3] expressed the belief that traumatic cerebral atrophy is a pressure atrophy due to a disturbance in the cerebrospinal fluid-eliminating mechanism (subarachnoid villi and pacchionian bodies), permitting an increase in the amount of supracortical fluid with pressure. As a result of Bagley's [4] observation of arachnoiditis produced from blood introduced into the subarachnoid spaces, Fay expressed the belief that cerebral trauma producing subarachnoid hemorrhage injures the pacchionian bodies, producing obstruction to the outflow of cerebrospinal fluid, with secondary pressure atrophy of the cortex.

When necropsy studies have been possible in cases of death resulting from some cause other than concussion, acute cerebral injury in the form of multiple punctate intracerebral hemorrhages has been shown. Osnato and Giliberti,[5] from a review of the literature and their own pathologic studies, found diffuse perivascular hemorrhagic infiltration similar to the perivascular pathology of acute encephalitis. They concluded that cases of concussion do show evidence of structural cerebral injury, and that there is a strong likelihood for secondary degenerative changes to develop. They believe, therefore, that postconcussion neuroses should properly be called traumatic encephalitis.

In mild cases of cerebral trauma that have been carefully observed from the onset, in which intracranial compression symptoms were mild and no pronounced cerebral edema was demonstrable on lumbar puncture and manometric reading and in which the spinal fluid was clear, marked pathologic changes have nevertheless been shown on later encephalography. The concept of traumatic encephalitis explains the pathologic findings better than Fay's concept of pressure atrophy from obstruction. As stated before, however, the combination of factors (cerebral edema, subarachnoid hemorrhage and intracerebral diffuse minute hemorrhages)

3. Fay, Temple: Generalized Pressure Atrophy of the Brain, Tr. Sect. Surg., Gen. & Abd., A. M. A., 1929, p. 186.

4. Bagley, Charles, Jr.: Blood in the Cerebrospinal Fluid: Resultant Functional and Organic Alterations in the Central Nervous System; A. Experimental Data, Arch. Surg. **17**:18 (July) 1928.

5. Osnato, M., and Giliberti, V.: Postconcussion Neurosis—Traumatic Encephalitis: A Conception of Postconcussion Phenomena, Arch. Neurol. & Psychiat. **18**:181 (Aug.) 1927.

probably produces the majority of cases of cortical atrophy. Obliterative arachnoiditis is best explained by previous subarachnoidal hemorrhage.

Variations in the size, contour and position of the ventricles result from a combination of atrophy of the brain and subarachnoidal changes which may produce traction through adhesions or pulsion through a cystic expansion of the supracortical channels. Atrophy of the parenchyma of the brain without peripheral fixation of the cortex by subarachnoidal adhesions or without a block between the ventricles and subarachnoidal spaces may lead to extensive widening of the arachnoidal channels and yet may cause little change in the ventricles. Asymmetric atrophy of the brain may lead to an unbalanced enlargement or distortion of the ventricles or subarachnoidal channels. Unilateral

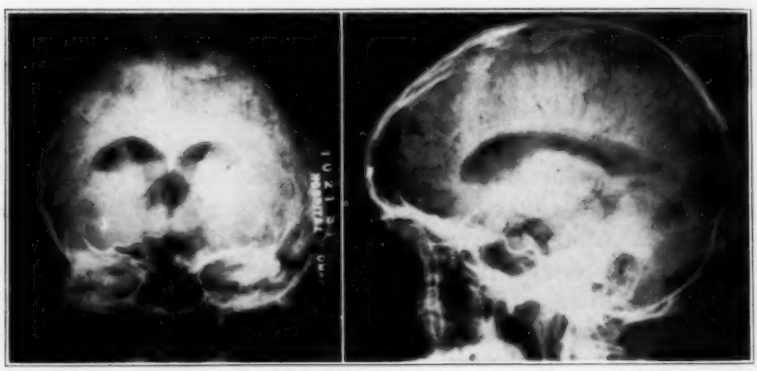

Fig. 1.—An essentially normal encephalographic study which shows clearly visualized subarachnoidal spaces distributed symmetrically over the cerebral cortex, about the cerebellum and through the basilar and cisternal channels without evident obliteration, enlargement or distortion. The ventricles are within the limits of normal size, position and contour.

adhesive arachnoiditis will tend to pull the ventricular system toward that side, while cystic expansion within the subarachnoidal or subdural region will tend to push the ventricles toward the opposite side. Symmetrical obliteration of the subarachnoidal spaces and absorption pathways, unattended by localized atrophy of the brain secondary to punctate hemorrhages, will lead to symmetrical atrophy of the brain with consequent symmetrical dilatation of the ventricles.

The following cases illustrate various pathologic findings on encephalography in cerebral trauma without fracture of the skull. These are the so-called cases of cerebral concussion or traumatic encephalitis. The cases also illustrate the marked benefit often obtained in the symptoms of the patient following spinal drainage with air replacement.

REPORT OF CASES [6]

CASE 1.—The birth of F. E., aged 17, had been a difficult breech delivery. The right arm had always been weak and underdeveloped. At 8 years of age he had received a severe kick in the head by a horse. Following this the patient was unconscious for about two hours and had fever for two days. Three weeks later Jacksonian convulsions began over the right half of the body, which became progressively worse. Neurologic examination was negative except for right homonomous hemianopia and spastic paresis of the right arm.

The clinical diagnosis was residual cortical defect from birth hemorrhage of the left rolandic area; secondary traumatic encephalitis.

Encephalography showed (fig. 2) atrophy of the left parietal and occipital lobes.

CASE 2.—Mr. G. W., aged 60, following an automobile accident in 1928, was semiconscious for one week. Progressive memory and a personality defect fol-

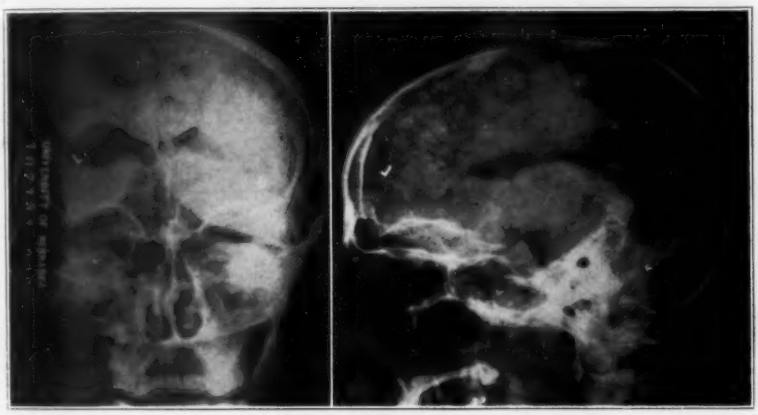

Fig. 2 (case 1).—Diffuse atrophy through the parenchyma of the brain, most extensive in the left parietal and occipital lobes of the cerebrum, thereby leading to an extensive local enlargement of the surrounding subarachnoidal space and an expansion of the posterior half of the left lateral ventricle. The right lateral ventricle and subarachnoidal channels are within normal limits. There is gross widening of the subtentorial space and cisterna magna suggestive of cerebellar atrophy.

lowed the injury. Examination in March 1930, revealed no focal signs of neurologic disease; a marked organic psychotic reaction type of psychosis was present.

The clinical diagnosis was cerebral arteriosclerosis with traumatic encephalitis.

Encephalography showed (fig. 3) obliterative arachnoiditis obstructing the basilar subarachnoid channels, with cortical atrophy.

CASE 3.—Mr. C. O., aged 22, had been in an automobile accident in January, 1931. This was followed by a period of unconsciousness in the hospital for seventeen days, but there was no fracture of the skull. He was mentally confused and amnesic for one month. When examined in April, 1931, the complaints were

6. Dr. G. Alexander Young gave us permission to report his cases 4 and 5. Dr. J. J. Keegan allowed us to report case 8.

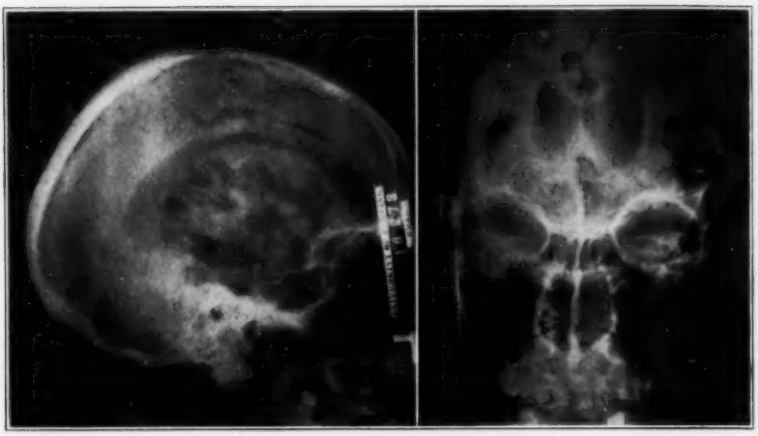

Fig. 3 (case 2).—Relatively complete obliteration of the supracortical subarachnoidal channels obstructing absorption of the cerebrospinal fluid and thereby leading to extensive widening of the more proximal subarachnoidal channels along the basilar and temporal regions together with a dilatation of the lateral ventricles and consequent parenchymal atrophy somewhat more extensive in the left side.

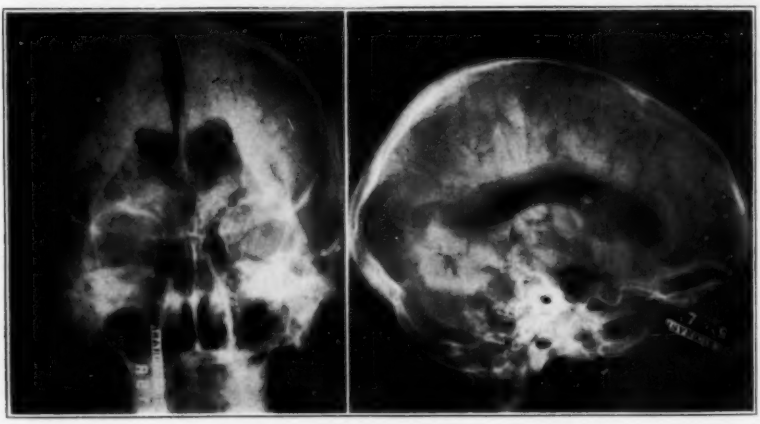

Fig. 4 (case 3).—Relative obliteration of the supracortical subarachnoidal channels, somewhat more complete over the left side of the cerebrum, leading to a moderate distention of the space along the falx and through the basilar cisterns together with dilatation of the lateral ventricles to four or five times the normal capacity and associated parenchymal atrophy, most extensive in the left side.

diplopia and headache. A partial palsy of the right third nerve was the only objective finding.

The clinical diagnosis was traumatic encephalitis and arachnoiditis.

Encephalography showed (fig. 4) bilateral obliterative arachnoiditis with cortical atrophy.

CASE 4.—Mr. H. C., aged 26, in June, 1931, suffered a compound fracture of the nasal bones from a heavy iron crank. The patient was unconscious for a few minutes, and remained in the hospital only three days. Following this he had continual frontal pain, which caused complete disability. Neurologic examination revealed no objective signs of organic disease, and traumatic hysteria was considered.

The clinical diagnosis was indeterminate. Encephalography was done for diagnosis.

Encephalography showed (fig. 5) obliterative arachnoiditis in the frontal areas with cortical atrophy.

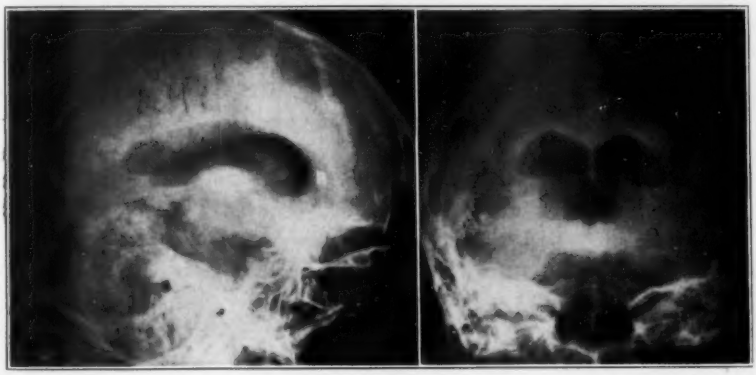

Fig. 5 (case 4).—Relative obliteration of the subarachnoidal spaces, most definitely pronounced over the frontal lobes and on the right side associated with slight cerebral atrophy and dilatation of the lateral ventricles, somewhat more extensive in the right frontal area, the lateral ventricle being four or five times the normal capacity.

Only a partial drainage was accomplished, which resulted in a transient improvement of symptoms. Three months later the patient had a second encephalographic study with complete drainage followed by complete relief from symptoms. The same obliterative arachnoiditis was present.

CASE 5.—Mr. L. E., aged 36, in April, 1931, was struck on the right parietal region with a rock weighing 4 pounds (1.8 Kg.) which fell 10 feet (300 cm.). Unconsciousness lasted about ten minutes. The accident was followed by pains in the head, vertigo and persistent nervousness, with an inability to lie on the back or the right side of the head. Neurologic examination revealed no organic signs.

The clinical diagnosis was indeterminate. Encephalography was done for diagnosis.

Encephalography showed (fig. 6) bilateral obliterative arachnoiditis and cortical atrophy. Complete relief from the headache and other symptoms followed the injection of air.

Case 6.—Mr. C. H., aged 40, had been in an automobile accident in August, 1931, in which he fractured his nose and was unconscious for about two hours. One week later he had febrile delirium for four days, and recovered when the right ear drum ruptured. Persistent headache and a purulent discharge from the ear continued. Examination on October 18 revealed purulent mastoiditis, lateral nystag-

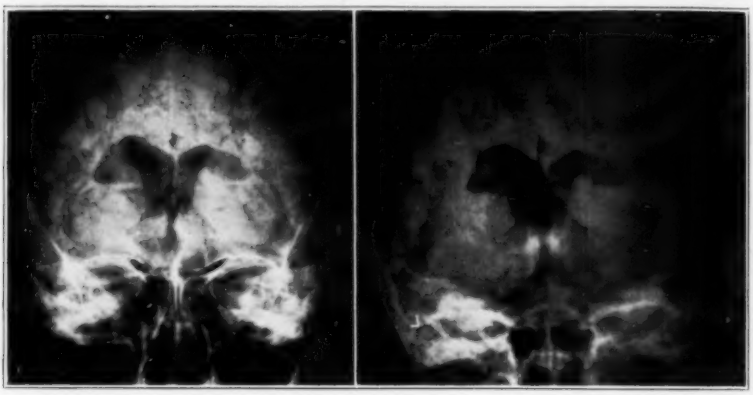

Fig. 6 (case 5).—Slight relative obliteration of the supracortical subarachnoidal channels, most definite over the left side of the cortex, together with enlargement of the left lateral ventricle to three or four times the normal size and with associated slight atrophy through the parenchyma of the left lobe of the cerebrum and slight atrophy through the right lobe.

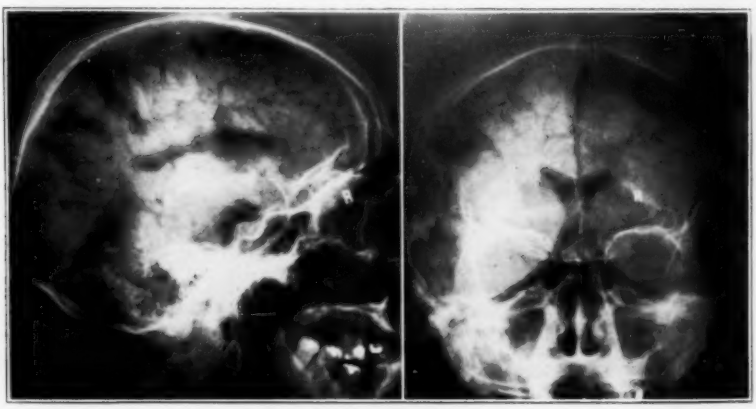

Fig. 7 (case 6).—Extensive bilateral generalized atrophy of the parenchyma of the cerebrum and cerebellum, leading to an expansion of the subarachnoidal channels over the cortex to a width of 10 or 20 mm. and a gross widening of the cisterna magna and subtentorial space. The ventricles appear normal in size and position, owing to the absence of peripheral fixation of the atrophic brain by adhesive obliterating arachnoiditis.

mus and an increased spinal fluid pressure. A simple mastoidectomy was performed without relieving the headache. A radical mastoidectomy was then performed on

account of the persistent drainage. Encephalography was then carried out on account of the persistent headache.

Encephalography showed (fig. 7) extensive bilateral cortical atrophy. Almost complete relief from symptoms followed the encephalography.

Fig. 8 (case 7).—Marked degree of generalized cortical atrophy leading to a slight widening of the subarachnoidal spaces over the cortex, but without enlargement of the ventricles.

Fig. 9 (case 8).—Extensive obliteration of the subarachnoidal channels about the right side of the cortex, with an associated density confluent with the lateral portion of the right side of the cerebrum. Moderate degree of atrophy through the parenchyma of the left side of the cerebrum, with an associated enlargement of the left ventricle to three or four times the normal size and slight displacement of the ventricles toward the left side.

Case 7.—Miss A. E., aged 18, four years previously had fallen on cement while roller skating and was unconscious for a few minutes. Severe headache and

vomiting were present for three days. Since that time the patient had suffered from petit mal seizures, vertigo, intense headaches and vomiting. During the past year the patient had been disabled from severe headache and daily vomiting. Examination revealed no objective findings except lateral nystagmoid movements; the cisternal fluid pressure was normal. The spinal fluid pressure with the patient in the upright position, prior to encephalography, was 40 mm. of mercury.

The clinical diagnosis was traumatic encephalitis.

Encephalography showed generalized bilateral cortical atrophy. This patient is still under observation, and is suffering from headache and vomiting; the spinal fluid pressure remains moderately increased. Subtemporal decompression is being considered to give relief.

CASE 8.—Mr. P. R., aged 24, in June, 1931, was thrown against an automobile steering wheel, but was not knocked unconscious. Gradually increasing headache, mental dulness and blurred vision developed. About five weeks after the onset, a subdural hematoma was drained through a right frontotemporal trephine opening. Spinal punctures had shown an elevated pressure. Temporary improvement followed the operation. Because of a recurrence of symptoms, encephalography was carried out on November 9 (fig. 9). On Dec. 3, 1931, Dr. J. J. Keegan performed a right subtemporal decompression, at which time thickened meninges, edematous cortex and flattened convolutions were found.

The clinical diagnosis was traumatic arachnoiditis from a previous subdural hematoma.

Encephalography showed (fig. 9) arachnoiditis and cortical atrophy.

SUMMARY

1. The importance of a more careful diagnostic study of the patient with mild cerebral traumatism is emphasized. In any doubtful case, the study should always include encephalography, which is the only accurate diagnostic method known. Encephalography should be recommended also as a therapeutic agent to relieve posttraumatic symptomatology.

2. The mechanism of production of cortical atrophy is discussed. The cause is usually a combination of factors: (*a*) an obstructive outflow of cerebrospinal fluid from subarachnoid hemorrhage and edema and (*b*) diffuse intracerebral punctate hemorrhages or traumatic encephalitis.

3. Eight illustrative case reports with encephalographic findings, showing pronounced cerebral damage from relatively minor injuries of the skull, are included. Therapeutic benefit in the relief of posttraumatic symptoms has been noted in about half of our cases.

EXPERIMENTAL ILEUS

III. PROLONGATION OF LIFE FOR SEVENTY DAYS AFTER HIGH INTESTINAL OBSTRUCTION BY ADMINISTRATION OF SODIUM CHLORIDE AND NUTRITIVE MATERIAL INTO INTESTINE BELOW THE SITE OF OCCLUSION

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Although most investigators and clinicians have attributed death in acute intestinal obstruction to a toxemia, there has been considerable evidence accumulating lately that supports the view that the loss of digestive secretions is an important factor in death from uncomplicated or simple high intestinal obstruction. Gatch, Trusler and Ayres [1] have emphasized the view held by Hausler and Foster [2] that two types of mechanical obstruction must be recognized: (1) acute simple obstruction in which there is simple occlusion of the lumen without circulatory involvement and (2) acute strangulation in which the obstruction is complicated by interference with venous, arterial or lymphatic circulation. As a result of their experiments Gatch and his associates concluded that in the first type, which occurs chiefly high up in the intestinal tract, death was caused by a profound metabolic disturbance resulting from three factors: dehydration, loss of chlorides and starvation. In the second type the same factors were present but were overshadowed by toxemia. They felt that the toxin was not absorbed from the intact mucosa but made its way into the circulation through an overdistended bowel, and in the event of gangrene the absorption by way of the peritoneal surface was rapidly fatal.

In this communication we are concerned with the loss of digestive secretions as an important factor in the explanation of death in uncomplicated high obstruction, and the evidence presented applies to this type

From the Department of Surgery, the University of Chicago.

1. Gatch, W. D.; Trusler, H. M., and Ayres, K. D.: Acute Intestinal Obstruction: Mechanism and Significance of Hypochloremia and Other Blood Chemical Changes, Am. J. M. Sc. **173**:649, 1927; Causes of Death in Acute Intestinal Obstruction, Surg., Gynec. & Obst. **46**:332, 1928.

2. Hausler, R. W., and Foster, W. C.: Studies of Acute Intestinal Obstruction: I. Different Types of Obstruction Produced Under Local Anesthesia, Arch. Int. Med. **34**:97 (July) 1924.

of obstruction. The appreciation that the mechanism of death probably is primarily chemical rather than toxic has been made possible by studies of the chemical composition of the blood of obstructed animals and also by experiments with fistulas. The most satisfactory explanation of the chemical nature of death resulting from loss of digestive secretions has been given in a series of articles by Gamble and McIver.[3] They found that the inorganic constituents of the digestive secretions were to a large extent sodium and chloride ion. The continued loss of these secretions depleted the blood plasma and interstitial fluids of the important blood electrolytes, fixed base (chiefly sodium) and chloride ions, without which the body could not hold fluids. Also the relative amounts of sodium and chloride ion lost resulted in an acidosis or an alkalosis of varying degree. They explained the mehanism of death on the basis of dehydration following loss of blood electrolytes, and of distortion of the acid-base equilibrium of the body. They believed that the loss of digestive secretions was an adequate explanation for the cause of death in uncomplicated high obstruction.

The evidence that the loss of digestive secretions is an important factor in the cause of death in high obstruction is offered by experiments involving: (1) administration of sodium chloride solution subcutaneously or intravenously to obstructed animals; (2) short-circuiting digestive secretions below the obstruction; (3) production of fistulas, high intestinal, pancreatic and gastric; (4) administration of substances into the bowel below the obstruction, such as vomitus, sodium chloride, dextrose and peptone.

Hartwell, Hoguet and Beekman [4] were the first to administer sodium chloride solution subcutaneously to animals with intestinal obstruction. By using about 500 cc. daily, they kept three animals with high obstruction alive from twenty-one to twenty-six days, when they were examined and killed. They felt that there were two important factors in death from high obstruction: 1. Loss of water from the tissues caused by excessive drainage into the intestinal lumen followed by vomiting.

3. McIver, M. A., and Gamble, J. L.: Body Fluid Changes Due to Upper Intestinal Obstruction, J. A. M. A. **91**:1589 (Nov. 24) 1928. Gamble, J. L., and McIver, M. A.: The Factor in the Dehydration Following Pyloric Obstruction, J. Clin. Investigation **1**:403, 1925; A Study of the Effect of Pyloric Obstruction, ibid. **1**:531, 1925; The Acid-Base Composition of Gastric Secretions, J. Exper. Med. **48**:837, 1928; The Acid-Base Composition of Pancreatic Juice and Bile, ibid. **48**:849, 1928; Body Fluid Changes Due to Continued Loss of the External Secretion of the Pancreas, ibid. **48**:859, 1928.

4. Hartwell, J. A.; Hoguet, J. P., and Beekman, F.: An Experimental Study of Intestinal Obstruction, Arch. Int. Med. **13**:701 (May) 1914. Hartwell, J. A., and Hoguet, J. P.: Experimental Intestinal Obstruction in Dogs with Especial Reference to the Cause of Death and the Treatment by Large Amounts of Normal Saline Solution, J. A. M. A. **59**:82 (July 13) 1912.

The administration of sodium chloride solution compensated for this loss. 2. The absorption of poisonous material from the intestinal wall when the mucosa was damaged. This factor was not influenced by the saline.

Studies of the chemical composition of the blood of animals with pyloric obstruction were first carried out by MacCallum and his co-workers.[5] They observed a fall in the blood chlorides and an increase in the alkali reserve which they ascribed to loss of gastric juice from vomiting. By treating these animals with sodium chloride solution, the marked changes in the chemical composition of the blood were prevented and life was prolonged. These observations were confirmed by Hastings, Murray and Murray.[6]

Haden and Orr [7] observed a fall in the blood chlorides associated with a rise in the carbon dioxide and nonprotein nitrogen in animals with high intestinal obstruction. This change in the chemical composition of the blood was prevented and life prolonged from three to four weeks by the administration of sodium chloride solution subcutaneously.[8] Death resulted even more rapidly in animals with obstruction that were given injections of distilled water than in those that were untreated.[9] They also found that other salts did not produce the same results as sodium chloride.[10] They concluded that the chloride in the blood was bound by the "toxin" and that the administration of sodium chloride acted as a neutralizer for the "toxin." This view, however, they have since altered and now recognize the "chemical" factors in death from obstruction.[11]

When a considerable part of the digestive secretions are short-circuited below the point of obstruction, animals will live a month.

5. MacCallum, W. G.; Lentz, J.; Vermilye, H. N.; Leggett, T. H., and Boas, E. J.: The Effect of Pyloric Obstruction in Relation to Gastric Tetany, Bull. Johns Hopkins Hosp. **31**:1, 1920.

6. Hastings, A. B.; Murray, C. D., and Murray, H. A.: Certain Chemical Changes in the Blood After Pyloric Obstruction in Dogs, J. Biol. Chem. **46**:223, 1921.

7. Haden, R. L., and Orr, T. G.: Chemical Changes in the Blood of the Dog After Intestinal Obstruction, J. Exper. Med. **37**:365, 1923.

8. Haden, R. L., and Orr, T. G.: The Effect of Sodium Chloride on the Chemical Changes in the Blood of the Dog After Pyloric and Intestinal Obstruction, J. Exper. Med. **38**:55, 1923.

9. Haden, R. L., and Orr, T. G.: Obstruction of the Jejunum: The Effect of Sodium Chloride on the Chemical Changes in the Blood of the Dog, Arch. Surg. **11**:859 (Dec.) 1925.

10. Haden, R. L., and Orr, T. G.: The Effect of Inorganic Salts on the Chemical Changes in the Blood of the Dog After Obstruction of the Duodenum, J. Exper. Med. **39**:321, 1924.

11. Orr, T. G., and Haden, R. L.: Chemical Factors in the Toxemia of Intestinal Obstruction, J. A. M. A. **91**:1529 (Nov. 17) 1928.

One of us (Dr. Jenkins [12]) kept an animal alive thirty-three days by simply short-circuiting the biliary, pancreatic and duodenal secretions beyond the point of a high obstruction. When the same procedure was done on animals with a low obstruction, the average length of life was ten days, although one animal lived twenty days.[13] When animals with a high obstruction on which the same short-circuiting procedure was carried out were given milk and cream along with some sodium chloride through a jejunostomy opening below the obstruction, life was prolonged to thirty-seven days.[14] Pearse [15] kept animals alive a month by short-circuiting the biliary, pancreatic and duodenal secretions and part of the gastric juice below the obstruction, and in addition he introduced milk and cream with some sodium chloride into the distal bowel through a gastrostomy tube in the pyloric part of the stomach. Apparently, there was enough gastric juice resorbed in the obstructed segment or enough diverted below the obstruction, as in Pearse's experiment, to prevent the usual rapidly fatal outcome of complete loss of gastric juice as in Dragstedt's isolated pouches of the entire stomach [16] or from pyloric obstruction.[6] The maintenance of the blood chlorides at a normal level during the period of obstruction when sodium chloride was added to the feedings was apparently due to the replacement of sodium and chloride ions that had been lost in the vomited gastric juice. These short-circuiting experiments are not convincing evidence in themselves that the loss of digestive secretions is an important factor in high obstruction; however, the results may be explained on that basis and warrant mention as such.

In support of the theory there is further evidence in the observations of the changes in the chemical composition of the blood and rapid death of animals that suffer from loss of digestive secretions from high intestinal, pancreatic or gastric fistulas. Walters, Kilgore and Bollman [17] found that in duodenal fistulas the changes in the

12. Jenkins, H. P.: Experimental Ileus: I. High Obstruction with the Biliary, Pancreatic and Duodenal Secretions Short-Circuited Below the Obstructed Point, Arch. Surg. **19**:1072 (Dec.) 1929.

13. Jenkins, H. P., and Roome, N. W.: Low Obstruction with the Biliary, Pancreatic and Duodenal Secretions Short-Circuited Below the Obstructed Point, Proc. Soc. Exper. Biol. & Med. **29**:395 (Jan.) 1932.

14. Jenkins, H. P.: Experimental Ileus: II. High Obstruction with the Biliary, Pancreatic and Duodenal Secretions, Along with Food and Sodium Chloride Entering Bowel Below Obstructed Point, Arch. Surg. **25**:849 (Nov.) 1932.

15. Pearse, H. E.: Is Toxaemia the Cause of Death in Uncomplicated Intestinal Obstruction? Ann. Surg. **93**:915, 1931.

16. Dragstedt, L. R., and Ellis, J. C.: The Fatal Effect of the Total Loss of Gastric Juice, Am. J. Physiol. **93**:407 (June) 1931.

17. Walters, W. Kilgore, A. M., and Bollman, J. L.: Changes in the Blood Resulting from Duodenal Fistula, J. A. M. A. **86**:186 (Jan. 16) 1926.

chemical composition of the blood were an increasing alkalosis, decreasing concentration of chlorides and a progressive rise in blood urea, and that death occurred in from three to four days. Life was prolonged for more than three weeks, and the changes in the chemical composition of the blood were prevented by the daily administration of from 500 to 700 cc. of 1 per cent sodium chloride solution intravenously. The administration of concentrated sodium chloride solution maintained the blood chlorides at a normal level but did not delay death. Dextrose solution (5 per cent) or sodium sulphate did not prolong life or prevent the changes in the chemical composition of the blood. The authors pointed out the similarity between duodenal fistula and high intestinal stasis, and were led to the conclusion that fluid balance played some part in the "toxemia" accompanying duodenal fistula.

Morton and Pearse [18] found that animals with a high obstruction or a high intestinal fistula at the same level died at approximately the same time and showed corresponding changes in the chemical composition of the blood. They felt that death was due to the same mechanism in both instances, i. e., loss of digestive secretions. Elman and Hartmann [19] also found that animals with a high intestinal fistula behaved practically the same as animals with obstruction at the same level (the lower end of the duodenum) as far as changes in the chemical composition of the blood and time of death were concerned. The changes in the chemical composition of the blood were prevented and life was prolonged by the injection of saline solutions in both instances. The mechanism of death was explained on the basis of "chemical changes in the body fluids resulting primarily from loss of gastrointestinal secretions, and secondarily from circulatory and renal insufficiency due to dehydration." They further stated that death in low obstruction was not due to such changes because the chemical composition of the blood was not markedly altered and saline did not appear to influence the length of life; also gangrene or necrosis of the bowel was not necessarily responsible for the lethal outcome.

Elman and McCaughan [20] found that the total loss of the external secretion of the pancreas was fatal in about a week. Elman and Hart-

18. Morton, J. J., and Pearse, H. E.: The Similarity in Effect of Experimental High Intestinal Obstruction and High Complete Intestinal Fistula, Ann. Surg. **94:** 263, 1931.

19. Elman, R., and Hartmann, A. F.: Experimental Obstruction of the Terminal Duodenum and Ileum: Importance of Blood Chemical Changes in Causing Death, Surg., Gynec. & Obst. **53:**307 (Sept.) 1931.

20. Elman, R., and McCaughan, J. M.: On the Collection of the Entire External Secretion of the Pancreas Under Sterile Conditions and the Fatal Effect of the Total Loss of Pancreatic Juice, J. Exper. Med. **45:**561, 1927.

mann [21] studied the chemical composition of the blood of animals with complete pancreatic fistulas and found a fall in chlorides and in the carbon dioxide. In animals that vomited considerably there was an alkalosis instead of an acidosis. These changes in the chemical composition of the blood were prevented by the administration of Ringer's solution, and life was prolonged. They felt that death was due to simple chemical changes brought about by a marked loss of base bicarbonate and a resulting uncompensated acidosis, and that dehydration was also a factor. Dragstedt and his co-workers [22] observed the same changes in the chemical composition of the blood in their experiments on pancreatic fistulas; they prolonged life by the administration of Ringer's solution. Dragstedt and Ellis [16] found that the complete loss of gastric juice from isolated pouches of the stomach was rapidly fatal and was associated with a marked fall in blood chlorides and alkalosis. The chemical composition of the blood remained normal and the life of the animals was prolonged over two months by the daily administration of Ringer's solution. Dragstedt,[23] following the observations on the rapidly fatal effect of the total loss of gastric or pancreatic juice, emphasized that the important factor in death from high intestinal obstruction was the result of failure of reabsorption of gastric and pancreatic juice because of their loss through vomiting.

The most convincing evidence is found in experiments in which material was introduced into the bowel through a jejunostomy opening below the obstruction. White and Fender [24] introduced the animal's vomitus along with water and dextrose into the bowel below the obstruction through a jejunostomy tube. Their animal lived a month. Matsukura [25] injected sodium chloride and water into a jejunostomy opening below the obstruction, and the animal lived thirty-three days. Armour and his co-workers [26] administered sodium chlo-

21. Elman, R., and Hartmann, A. F.: The Cause of Death Following Rapidly the Total Loss of Pancreatic Juice, Arch. Surg. **20**:333 (Feb.) 1930.

22. Dragstedt, L. R.; Montgomery, M. L.; Mathews, W. B., and Ellis, J. C.: Fatal Effect of the Total Loss of Pancreatic Juice, Proc. Soc. Exper. Biol. & Med. **28**:110, 1930.

23. Dragstedt, L. R.: Failure of Reabsorption of Gastric and Pancreatic Juice, Am. J. Surg. **11**:544, 1931.

24. White, J. C., and Fender, F. A.: The Cause in Uncomplicated High Intestinal Obstruction, Arch. Surg. **20**:897 (June) 1930.

25. Matsukura, S.: Chemical Studies on Liver and Other Tissues in Intestinal Obstruction, Closed Loop, Intestinal Fistula, and Perforative Peritonitis, Jap. J. M. Sc. (Tr. Surg. Orthod. & Odont.) **2**:1, 1930.

26. Armour, J. C.; Brown, T. G.; Dunlop, D. M.; Mitchell, T. C.; Searles, H. H., and Stewart, C. P.: Studies on High Intestinal Obstruction: The Administration of Saline and Other Substances by Enterostomy Below Site of Obstruction, Brit. J. Surg. **18**:467, 1931.

ride, dextrose, peptone, water and other substances into a jejunostomy opening below the obstruction. One of their animals lived fifty days. They stressed the point that the withdrawal of sodium chloride from the feedings during the obstructed period would cause death in a few days, with the usual changes in the blood chemistry of untreated obstruction, whereas when the animal was getting sodium chloride, the chemical composition of the blood remained normal. One animal was killed on the forty-fifth day by withdrawing the sodium chloride two days previously, and another had the sodium chloride withdrawn on the forty-fifth day until the changes in the blood chemistry were marked and the animal's condition was obviously critical, when salt was again administered on the forty-seventh day. The condition of the animal improved, and the figures for the chemical composition of the blood returned to normal. This animal had the continuity of the bowel reestablished on the fiftieth day, and from then on improved rapidly. It is probable that the animal would have lived considerably longer than fifty days with the obstruction if the continuity of the bowel had not been reestablished at that time. The work of Armour and his associates was published shortly after the preliminary report [27] of this experiment, in which an animal was kept alive for fifty-two days by the daily administration of about a liter of 1 per cent sodium chloride and 5 per cent dextrose solution into the bowel below the obstruction. Since this report we have kept an animal alive for seventy days by adding peptonized milk to the salt and dextrose feedings.

EXPERIMENTATION

Technic.—The dogs, after being received from the pound, were kept for from two to three weeks in isolation to eliminate distemper. The operations were done under morphine-ether anesthesia. A small left rectus incision was made and the jejunum just beyond the ligament of Treitz delivered. The jejunum was sectioned at varying distances from the ligament of Treitz in the different animals by clamping, ligating, cutting and invaginating the stumps with a linen purse-string suture. The distal stump was always brought to the outside through a stab wound in the right rectus and sutured to the skin (fig. 1). The stump brought to the outside was usually opened at operation after the incision was closed, but in some animals it was not opened until the following day. As soon as the stump was opened, the animal was given from 1,000 to 1,350 cc. of 1 per cent sodium chloride and from 5 to 7 per cent dextrose daily, administered from eight to ten times a day at from an hour and a half to two hour intervals. Occasionally 2 per cent sodium chloride was used for the first few days after operation. When dextrose was given in concentrations greater than 7 per cent, a watery diarrhea usually developed. The weights were taken daily. Determinations of the chemical composition of the blood were made every week or ten days. A control series was obstructed in the same

27. Jenkins, H. P.: Prolonging Life in High Obstruction by Administration of Salt Solution Below Point of Obstruction, Proc. Soc. Exper. Biol. & Med. **28**: 111, 1930.

manner and treated by giving them about a liter of distilled water daily through the jejunostomy opening.

Concerning the chemical composition of the blood, the carbon dioxide capacity or combining power of the plasma was determined in volume per hundred cubic centimeters by the van Slyke method. The total whole blood chlorides were

Fig. 1.—Diagram of the operative procedure.

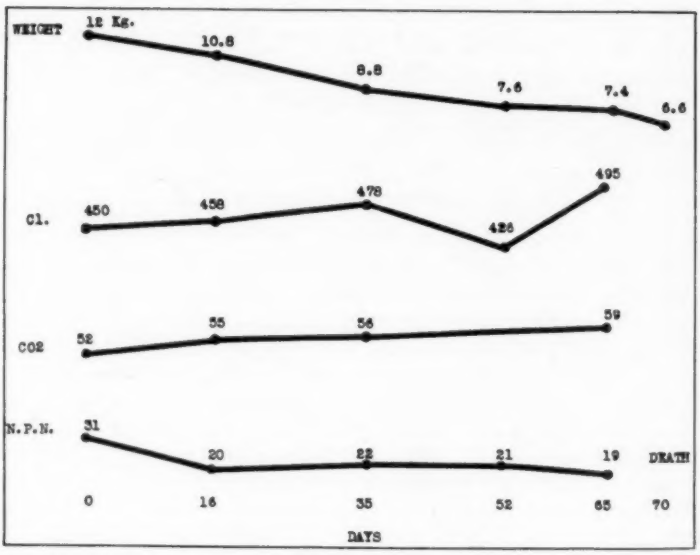

Fig. 2 (dog 660).—Curves of the weight and the figures for the chemical composition of the blood.

estimated as sodium chloride by Whitehorn's modification of Volhard's method. The determinations of nonprotein nitrogen were made by Koch and McMeekin's method.

Protocols.—Series I: Treated with Saline and Nutritive Material Introduced into the Jejunostomy Opening.

Dog 660: The obstruction was made 23 cm. from the pylorus. During the first four days a liter of 1 per cent sodium chloride and 6 per cent dextrose was given through the jejunostomy opening in from eight to nine feedings. From the fifth day on the animal was given approximately 500 cc. of sodium chloride mixture and 500 cc. of peptonized milk. (This was made by adding 1 tube of Fairchild and Foster's peptonizing substance to a pint of milk.) The relative amounts of the salt-dextrose solution and peptonized milk varied occasionally. The animal vomited on thirty-one of the seventy days. The amount of vomitus was not measured because

Fig. 3 (dog 660).—Specimen from the dog, which lived seventy days. The obstructed bowel measured 23 cm.

it was mixed with the urine in the cage. Small formed stools were passed two or three times a week. The weight gradually declined from 12 Kg. before operation to 6.6 Kg. on the seventieth day. This was a loss of 0.0771 Kg., or 0.642 per cent, per day. Studies of the chemical composition of the blood (fig. 2) showed relatively little change during the period of obstruction. The chlorides showed a slight rise from 450 to 495 mg. The nonprotein nitrogen dropped from 31 to 19 mg., and the carbondioxide fluctuated from 52 to 59 mg. The animal showed signs of weakness during the last week which progressed rapidly until the seventieth day, when it was killed while practically moribund. At autopsy a small patch of bronchopneumonia was found. There was no other explanation for the impending death other

than the emaciation from the long-standing obstruction. The 23 cm. of obstructed bowel and the stomach were moderately dilated (fig. 3).

Dog 533: The obstruction was made at a point 95 cm. from the pylorus. It was given 700 cc. of 1 per cent sodium chloride during the first sixteen days. From the seventeenth day on it received 1,000 cc. of 1 per cent sodium chloride and 5 per cent dextrose daily. The feedings were given in 100 cc. amounts at from one and a half to two hour intervals. Vomiting occurred on the average of every other day. Occasionally a slight diarrhea was noticed when the dextrose was poorly tolerated. From the eleventh to the thirteenth day the animal received 200 cc. of milk by mouth daily. On the twenty-eighth and thirty-first days, 300 cc. of milk was also given by mouth. On the fifty-first day, gastric analysis showed no free acid and a combined acid of 27 points. The weight gradually declined from

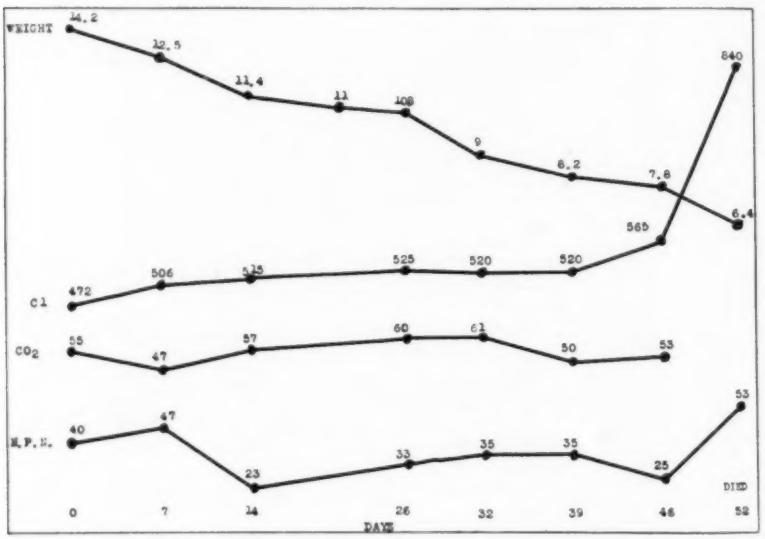

Fig. 4 (dog 533).—Curves of the weight and the figures for the chemical composition of the blood.

14.2 Kg. before operation to 6.4 Kg. on the fifty-second day. This was an average loss of 0.15 Kg., or 1.05 per cent daily of the original body weight. Analyses of the chemical composition of the blood (fig. 4) showed a very slight rise in chlorides during the first thirty-nine days, from 472 to 520 mg. On the forty-sixth day, the chlorides went up somewhat higher, to 565 mg., and on the day of death (fifty-second day) the reading was 840 mg. The carbon dioxide fluctuated only slightly from the preoperative determination of from 55 to 53 mg. on the forty-sixth day. The nonprotein nitrogen was originally 40 mg., but after a slight rise to 47 mg. at the end of the first week it dropped to 23 mg. at the end of the second week. It then fluctuated slightly until the fifty-second day, when it was 53 mg. The behavior of the animal was apparently practically normal until a few days before death, when it appeared to be quite weak. Death occurred on the fifty-second day. At autopsy there was no demonstrable cause of death other than the long-standing obstruction and the severe emaciation from starvation. There was practically no adipose tissue in the subcutaneous, omental, mesenteric or perirenal

regions. The blood count taken at time of death showed a hemoglobin of from 75 to 80 per cent, a red count of 3,050,000 and a white count of 6,400. The urine showed some albumin along with a few red cells and pus cells. The obstructed portion of the bowel measured 95 cm. from the pylorus, and was distended to a diameter of 5.5 cm. in the distal 30 cm. (fig. 5). The wall was enormously hypertrophied in the distal 15 cm. In the proximal part in the region of the duodenum the diameter varied from 1.7 to 2 cm. The stomach was not distended. The bowel from the jejunostomy opening to the cecum measured 80 cm. in length and varied from 1.2 to 1.8 cm. in diameter.

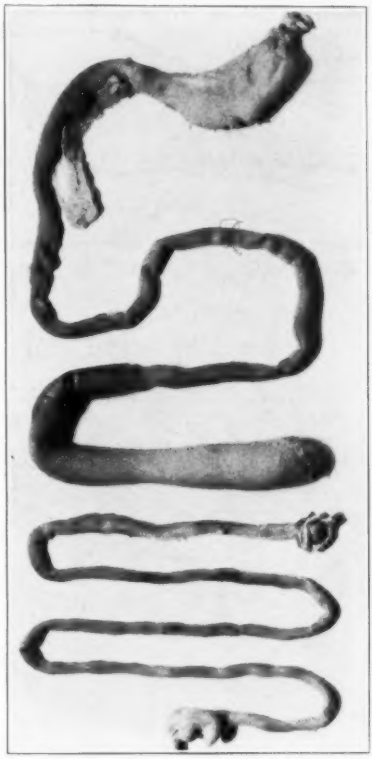

Fig. 5 (dog 533).—Specimen from the dog, which lived fifty-two days. The obstructed bowel measured 95 cm.

Dog 575: The obstruction was produced 42 cm. from the pylorus. During the first four days the animal received daily an average of 1,350 cc. of 2 per cent sodium chloride. On the fifth day 7 per cent dextrose and 1 per cent sodium chloride solution were started, and approximately 1,200 cc. was given daily in from eight to ten feedings. Vomiting occurred on at least twenty-two of the thirty-eight days of the period of obstruction. On five occasions a small stool was passed The weight gradually declined from 17.4 to 10 Kg. on the thirty-eighth day, when the animal died. This was an average daily loss of 0.19 Kg., or 1.12 per cent. The chemical composition of the blood showed relatively little change during the obstruction (fig. 6). The blood chlorides were 553 mg. before operation and fluc-

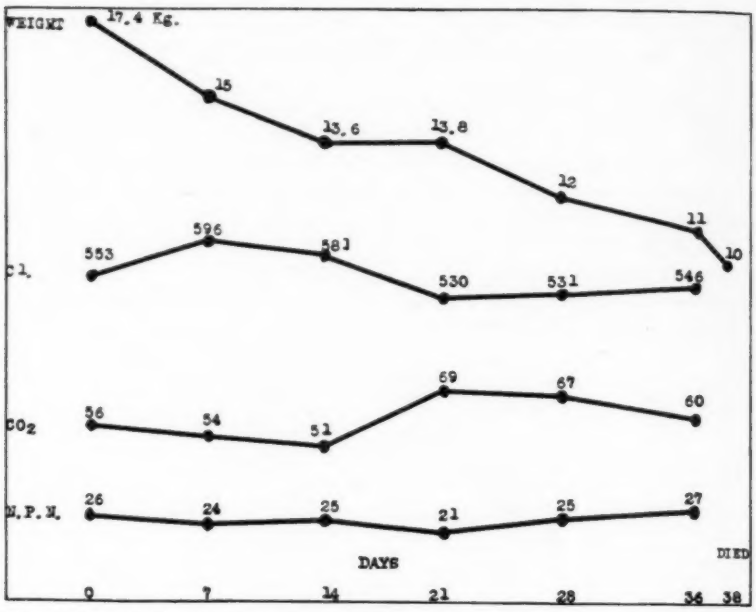

Fig. 6 (dog 575).—Curves of the weight and the figures for the chemical composition of the blood.

Fig. 7 (dog 575).—Specimen from the dog, which lived thirty-eight days. The obstruction was 42 cm. from the pylorus.

tuated slightly up to the thirty-sixth day, when they were 546 mg. The carbon dioxide started at 56 mg. and rose to 69 mg. on the twenty-first day, but came down to 60 mg. on the thirty-sixth day. The nonprotein nitrogen started at 26 mg. and ended at 27 mg. on the thirty-sixth day. The general condition of the animal was good until the thirty-sixth day, when weakness was noticed which became progressively worse until death occurred on the thirty-eighth day. Autopsy revealed a definite bronchopneumonia that was sufficiently extensive to explain completely the immediate cause of death. The stomach and 42 cm. of obstructed bowel were distended (fig. 7). The most marked distention of the bowel was just above the obstruction, where the diameter measured 4 cm. There were 205 cm. of small bowel between the jejunostomy and cecum, which was collapsed.

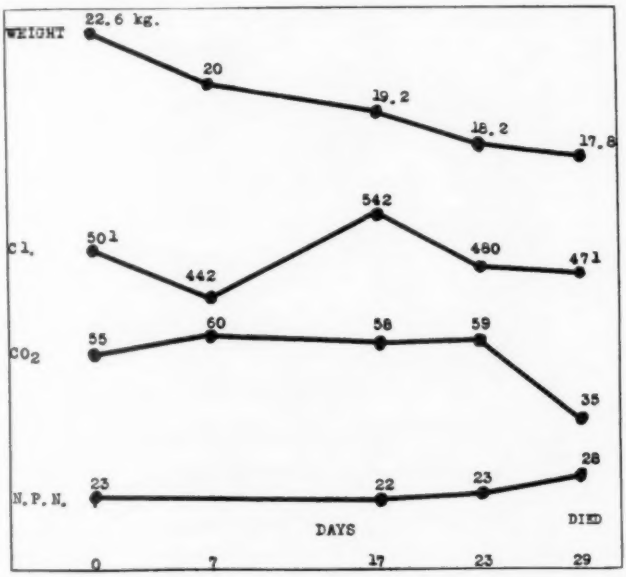

Fig. 8 (dog 664).—Curves of the weight and the figures for the chemical composition of the blood.

Dog 664: In this animal the obstruction was made 50 cm. from the pylorus. About 800 or 1,000 cc. of 1 per cent sodium chloride and 7 per cent dextrose solution was given in from seven to eight feedings daily except for the first two days, when only 2 per cent sodium chloride was used. Vomiting occurred on at least fifteen of the twenty-nine days. The weight declined from 22.6 to 17.8 Kg. This was an average loss of 0.165 Kg. per day, or 0.72 per cent of the original body weight daily. Chemical analysis of the blood showed a change in chlorides from 501 mg. before operation to 471 mg. on the twenty-ninth day (fig. 8). The carbon dioxide started at 55 mg. and stayed at from 58 to 60 mg. until the twenty-third day, and then fell to 35 mg. on the day of death. The blood was taken for chemical determinations two hours before death. The nonprotein nitrogen showed only a slight rise from 23 to 28 mg. The general behavior of the animal was excellent until the twenty-eighth day when it appeared rather weak. On the twenty-ninth day there was a marked change; the animal was spastic and had several convulsions. The animal was unable to stand up, and when molested was seized with convulsions during one

of which it died. At autopsy there was no demonstrable explanation for the cause of death other than the presence of the obstruction. The animal showed little evidence of emaciation as the adipose tissue of the omentum and mesentery was well preserved. There was moderate dilatation of the stomach and 50 cm. of obstructed bowel (fig. 9). The bowel from the jejunostomy to the cecum measured 150 cm.

Dog 99: The obstruction was produced 75 cm. from the pylorus. This animal was given 1,000 cc. of 2 per cent sodium chloride in six feedings daily for the first

Fig. 9 (dog 664).—Specimen from the dog, which lived twenty-nine days. The obstruction was 50 cm. from the pylorus.

three days. After this 1 per cent sodium chloride and 5 per cent dextrose were used, and the feedings were given nine times a day. The weight gradually fell from 10 to 6.3 Kg. on the twenty-sixth day, when the animal died. This was an average daily loss of 0.127 Kg., or 1.27 per cent. The blood chlorides, which were originally 520 mg., showed relatively little change during the first two weeks; however, on the twenty-sixth day, the reading was 819 mg. (fig. 10). The carbon dioxide fluctuated slightly from 62 mg. before operation to 59 mg. on the twenty-fifth day. The nonprotein nitrogen rose from 25 to 34 mg. on the last day. Vomiting was noticed on at least fourteen days. The animal showed very little premonitory sign of death. Autopsy revealed a leak in the obstructed bowel at the

site of the invaginated stump which had produced a generalized peritonitis. The obstructed bowel was only moderately distended just above the obstruction.

Dog 168: In this animal the obstruction was made 60 cm. from the pylorus. It was given 1,100 cc. of 2 per cent sodium chloride through the jejunostomy opening during the first two days, and thereafter the same amount of 1 per cent sodium chloride and 7 per cent dextrose in from eight to nine feedings daily. The weight declined from 20 to 16.2 Kg. on the twenty-fifth day, when the animal died. For two days previous to death the animal appeared to be definitely spastic. Clinical analysis of the blood showed relatively little change. The chlorides were 482 mg. before operation, and 539 mg. on the twenty-fifth day. The carbon dioxide was 57 mg. before operation and 53 mg. on the last day. The nonprotein nitrogen

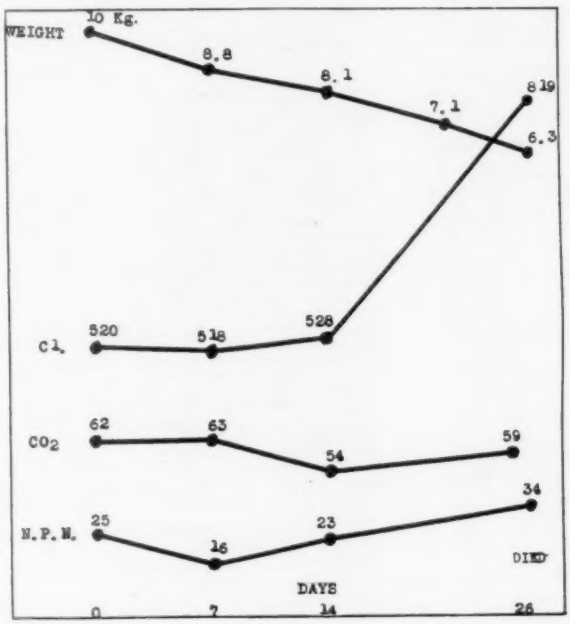

Fig. 10 (dog 99).—Curves of the weight and the figures for the chemical composition of the blood.

changed only from 25 to 27 mg. The last blood was drawn for chemical determinations ten hours before death. Autopsy revealed moderate distention of the obstructed bowel, especially at the distal end. The stomach was not especially distended. There was a patch of bronchopneumonia in the lower lobe of the right lung, which was relatively small. There was some question as to whether this was adequate to explain completely the cause of death.

Dog 170: The obstruction was produced 55 cm. from the pylorus. About 1,200 cc. of 1 per cent sodium chloride and 6 per cent dextrose was given daily in nine feedings. The weight declined from 16.5 to 12.4 Kg. on the twenty-first day, when the animal died. The chemical composition of the blood was determined only up to the fifteenth day. The blood chlorides were 620 mg. before operation, and, after a sharp rise to 826 mg. on the eighth day, fell to 678 mg. on the fifteenth day. The carbon dioxide changed from 61 to 54 mg. and the nonprotein nitrogen rose from 25

to 30 mg. at the end of two weeks. Autopsy showed a marked bronchopneumonia and moderate distention of the obstructed bowel.

Dog. 5: The obstruction was produced 30 cm. from the pylorus. About 900 cc. of 1 per cent sodium chloride and 5 per cent dextrose was given daily in nine feedings. The weight declined from 7.8 Kg. before operation to 5.3 Kg. on the seventeenth day, when the animal died. The blood chemistry taken up to the fourteenth day showed no marked changes. The chlorides rose from 502 to 614 mg.; the carbon dioxide changed from 45 to 48 mg., and the nonprotein nitrogen dropped from 30 to 19 mg. Autopsy showed a rather extensive localized peritonitis about the end

TABLE 1.—*Length of Life and Autopsy Observations in Series of Thirty-Eight Dogs with High Obstruction Treated by Saline Administered into the Jejunostomy Below the Obstruction*

Dog	Length of Life, Days	Autopsy Observations
660	70	Small patch of bronchopneumonia and emaciation
533	52	Emaciation
575	38	Bronchopneumonia
664	29	No findings (unexplained convulsions)
99	26	Generalized peritonitis from leak at obstructed stump
168	25	Small patch of bronchopneumonia
170	21	Bronchopneumonia
5	17	Localized peritonitis about obstructed stump
721	15	Bronchopneumonia (following resuture of wound)
811	13	Bronchopneumonia
655	11	Small patch of bronchopneumonia
577	8	Generalized peritonitis from perforation of bowel
658	8	Bronchopneumonia (following resuture of wound)
893	8	Generalized peritonitis
894	8	Bronchopneumonia
733	7	Generalized peritonitis and bronchopneumonia
83	6	Bronchopneumonia
173	6	Distemper and bronchopneumonia
491	5	Pulled jejunostomy stump out
661	5	Bronchopneumonia
923	5	Pulled jejunostomy stump out
2	4	Pulled jejunostomy stump out
322	4	Distemper (electrocuted)
325	4	Bronchopneumonia
534	4	Pulled jejunostomy stump out
660	4	Generalized peritonitis from perforation of bowel
327	3	Pulled jejunostomy stump out (electrocuted)
425	3	No findings
428	3	No abdominal or chest findings, some edema of brain
490	3	Generalized peritonitis
810	3	Pulled jejunostomy stump out
918	3	Generalized peritonitis
222	2	Bronchopneumonia
225	2	Pulled jejunostomy stump out
326	2	Bronchopneumonia
732	2	Generalized peritonitis
920	2	Bronchopneumonia
921	2	Localized peritonitis and gangrene of jejunostomy loop

of the obstructed stump of the jejunum. There was no definite evidence of a generalized peritonitis.

In addition to the eight animals the protocols of which are given, in thirty other dogs obstructions were produced in the upper jejunum and the animals were treated with sodium chloride and dextrose solution, which was injected into the bowel below the obstruction (table 1). The length of life of the thirty animals not included in the protocol was considerably shortened. One dog died on the fifteenth day, another on the thirteenth and still another on the eleventh. Four died on the eighth day, 1 on the seventh, and two on the sixth. Three died on the fifth day and five on the fourth. Six animals died on the third day, and another six on the second day. In this series of thirty animals the autopsy observations were pulmonary infection, thirteen; peritoneal infection, seven; pulling out of jejunostomy

stump and evisceration, seven; pulmonary and peritoneal infection, one. In two the observations were not adequate to explain death, and in one, listed under pulmonary infection, the patch of bronchopneumonia was relatively small and did not appear sufficiently extensive completely to explain death.

Series II: Treated with Distilled Water Introduced into the Jejunostomy Opening (control).

In a series of four animals an obstruction was produced in the upper jejunum in the same manner as in the previous series. The dogs were given approximately 1,000 cc. of distilled water daily through the jejunostomy opening in from eight to nine feedings. Nothing was given by mouth. The dogs lived five, six, eight and eleven days. The changes in the chemical composition of the blood were rather slight in the animals that lived five and six days; however, marked changes were observed in the two that lived eight and eleven days (table 2). The most noticeable change was seen in dog 190, in which the blood chlorides fell to 212 mg., the

TABLE 2.—*The Weight, Chemical Composition of the Blood, Time of Death and Length of Obstructed Bowel in Water Control Series*

				Chemical Composition of the Blood			
	Lived	Weight	Distance of Obstruction From Pylorus	Day	Chloride, Mg.	Carbon Dioxide, Mg.	Nonprotein Nitrogen, Mg.
Dog 76.....	5 days	21 Kg.	50 cm.	0	459	47	32
				3	419	49	45
Dog 189.....	6 days	17 Kg.	45 cm.	0	495	49	23
				3	465	53	23
				5	416	57	28
Dog 657.....	8 days	13 Kg.	45 cm.	0	528	54	33
				2	495	48	23
				5	407	64	31
				7	317	71	92
				8	288	52	133
Dog 190.....	11 days	16 Kg.	45 cm.	0	447	50	33
				3	384	57	38
				5	341	70	37
				7	291	79	51
				9	242	80	80
				10	212	84	118

carbon dioxide rose to 84 mg., and the nonprotein nitrogen rose to 118 mg. At autopsy there were no demonstrable observations other than the obstruction to explain death.

COMMENT

The marked prolongation of life in high obstruction that was obtained in this experiment with relatively slight changes in the chemical composition of the blood was apparently due primarily to the replacement, in the form of sodium chloride solution, of the water and important blood electrolytes, fixed base (chiefly sodium) and chloride ions, which were lost in the vomited digestive secretions; secondarily to the addition of nutritive material which helped to ward off starvation: dextrose, plus peptonized milk in one instance. The blood chlorides remained at a normal level in all the obstructed animals except three (dogs 533, 99 and 170), in which there was a marked rise. In the experiments of Gatch, Trusler and Ayres[1] several instances of

a rise in blood chlorides were observed when the animals in which obstructions were produced were treated by sodium chloride solution subcutaneously or intravenously. One animal with a low ileal obstruction, which received 1.8 per cent sodium chloride subcutaneously in from 1,000 to 2,000 cc. amounts daily and died on the twenty-first day, had a terminal blood (sodium) chloride of 830 mg. Another animal with a duodenal obstruction, which received 30 cc. of 33 per cent sodium chloride solution intravenously daily, died on the third day with a blood (sodium) chloride of 724 mg. Denis and Sisson [28] were able to produce a rise of 18 per cent in the blood chlorides of goats after the ingestion of large amounts of sodium chloride by mouth. It is possible that the high blood chlorides that were observed in three instances in this experiment were due to the administration of more sodium chloride than was actually needed by the animal to replace the lost electrolytes.

The replacement of water without the blood electrolytes does not delay the usual rapid death or prevent entirely the characteristic chemical changes of the blood in high obstruction. The dogs in the water control series died in five, six, eight and eleven days, and marked changes were observed in the blood chemistry of the two that survived the longest. In the experiments of Saito, Sakai and Suzuki [29] an animal with an obstruction of the duodenum was treated by instilling 1,000 cc. of water daily into the bowel below the obstruction. This animal lived two days and showed a fall in the blood chlorides from 517 to 337 mg., and a rise in nonprotein nitrogen from 40 to 250 mg. Matsukura [25] also had an animal that lived two days after the same procedure. In this instance the blood chlorides fell from 516 to 292 mg. Haden and Orr [9] found that distilled water injected subcutaneously into animals with an obstruction caused death even more rapidly than it occurred in untreated animals. Gatch, Trusler and Ayres [1] observed this also, but further found that animals without obstruction also died following the injection of distilled water.

Gatch, Trusler and Ayres [1] found that the intravenous injection of concentrated sodium chloride solution prevented a marked fall in the blood chlorides in obstruction but did not appreciably delay death. Haden and Orr also found that concentrated sodium chloride solution restored the blood chlorides to normal, but they felt that it had a definitely beneficial effect in the recovery of animals in which obstruction had been produced when the obstruction was subsequently relieved by a second operation. Nevertheless, they did not report any instances

28. Denis, W., and Sisson, W. R.: A Study of the Chlorine Content of Milk and Blood After Ingestion of Sodium Chloride, J. Biol. Chem. **46**:483, 1921.

29. Saito, S.; Sakai, K., and Suzuki, S.: Further Studies on Acute Intestinal Obstruction, Jap. J. M. Sc. (Tr. Surg. Orth. & Odont.) **1**:43, 1927.

of marked prolongation of life by injections of concentrated salt solution as they did with injections of diluted solutions. Haden and Orr [10] further demonstrated that the injection of other chloride salts, such as ammonium, potassium, calcium or magnesium chloride, did not prevent the usual fall in blood chlorides or delay the fatal outcome. Neither did numerous other salts, such as iodides, sodium bromide, sodium sulphate, magnesium sulphate, sodium citrate, monosodium phosphate and disodium phosphate, have any beneficial effect in preventing the chemical changes in the blood or in delaying death.

It appears that there are two important primary factors necessary to prolong life in high obstruction: replacement of water and replacement of the blood electrolytes by sodium chloride salt. The replacement of one without the other appears to have relatively little value, because the dehydration that occurs in obstruction is due not only to the loss of water, but also to the loss of the blood electrolytes that the body needs to hold water, even if it is replaced.

In regard to the effect of dextrose, it appears that its value is only nutritive. Haden and Orr [8] found that there was no demonstrable beneficial effect in preventing the changes in the chemical composition of the blood or in delaying death from the administration of dextrose solution subcutaneously to an animal with an obstruction. Saito, Sakai and Suzuki [29] introduced 1,000 cc. of 5 per cent dextrose daily into the bowel below the point of a duodenal obstruction. Their animal lived six and one-half days and showed a fall in the blood chlorides from 495 to 238 mg. and a rise in nonprotein nitrogen from 20 to 40 mg. In the experiments of Matsukura,[25] a similarly obstructed and treated animal lived four days and showed a fall in blood chlorides from 495 to 305 mg. It appears that dextrose solution may replace water, but this without the blood electrolytes is valueless and the dextrose itself has no beneficial effect except as a nutritive agent. The 50 to 70 Gm. of dextrose given to the animals daily in this experiment offers from 200 to 280 calories a day that would not otherwise be available. In the instance of the animal given peptonized milk, this added calories to the diet and helped the state of nutrition by its protein content, although it was probably not all sufficiently split to permit complete absorption in the bowel.

The loss of weight observed in the animals in this experiment varied considerably. The daily average loss varied from 0.0771 to 0.195 Kg., and the daily loss calculated in percentage of the original body weight varied from 0.642 to 1.88 per cent. In an experiment by Kunde,[30] a series of three animals that were simply starved for from thirty-seven

30. Kunde, M. M.: The After Effect of Prolonged Fasting on the Basal Metabolic Rate, J. Metab. Research **3**:399, 1923.

to forty-one days, the loss of weight averaged 0.117 Kg., or 1.01 per cent, per day. The effect of the dextrose was apparently not very great and in some instances valueless in preventing loss of weight from the starvation of obstruction. In the animal that Armour and his associates [26] kept alive for fifty days, the loss of weight was 0.71 per cent of the original body weight daily, which compares favorably with two of the animals in our series (dogs 168 and 664). A more complete diet was used in Armour's experiment than was used in any of our animals. In the dog that we kept for seventy days, the loss of weight was the least, 0.071 Kg., or 0.642 per cent, daily. The maximum beneficial effect of the nutritive material in our experiment and in Armour's has been to prevent approximately a third of the daily loss of weight that occurs from starvation alone.

The death that ultimately results was found to be definitely due to a complication in most of the animals. This is not surprising when one considers that the resistance of the animals is probably markedly lower to infections, especially pulmonary, as a result of the starvation alone, which is only partially combated by the administration of nutritive material in this experiment, which at best would not have been adequate to maintain a balanced state of nutrition. In one animal (dog 575) that lived twenty-nine days the explanation for the cause of death was obscure. There was no alteration in the blood chlorides or nonprotein nitrogen just before death; however, there was marked acidosis. The premonitory symptoms were those of spasticity and convulsions. The anatomic observations revealed nothing to explain death satisfactorily. The general state of nutrition of the animal was apparently good, because the mesenteric and omental adipose tissue was well preserved. It is not easy to say whether the acidosis was responsible for the convulsions or was merely another evidence of a profound metabolic disorder. Another animal (dog 169) behaved similarly toward the end, and a patch of bronchopneumonia was found at autopsy which did not seem adequate completely to explain death because of its small size. The chemical composition of the blood was practically the same on the day of death as before operation. Kunde [30] described marked manifestations of the central nervous system in one of three animals that were starved longer than a month. It is possible that death in the two animals in this experiment, which showed marked nervous manifestations just before, may have been due to a metabolic disorder of nutrition from deficiency in some organic or inorganic substance necessary for life. This may have been accidentally supplied to the other animals that lived longer, because most of the other animals occasionally had some food by mouth. After about a month on an artificial diet of sodium chloride and dextrose, this factor may become important. In

the series of thirty-eight animals in which obstructions were produced and the animals treated with saline and dextrose, there were two that died in three days without any demonstrable changes at autopsy other than the presence of the obstruction which would adequately explain death. These animals were operated on during a very hot spell of weather, and it is possible that heat prostration may have had something to do with the early death. On the other hand, death may have been due to the obstruction even though the dogs were receiving sodium chloride the same as the other animals. This, of course, opens the question as to whether or not there is a factor in death from high obstruction other than the loss of digestive secretions which under some circumstances may kill the animal even if the constituents of the lost secretions are replaced. This factor may have been responsible for the death of other animals (dogs 575, 168, 655 and 5). One of these (dog 5) died on the seventeenth day, showing only an area of localized peritonitis about the obstructed stump. The animal that lived fifty-two days (dog 533) showed a marked hyperchloremia on the day of death. There was no demonstrable complication found at autopsy, and the only explanation that can be offered other than the presence of the obstruction was profound emaciation from loss of over half its original body weight. The animal that lived seventy days (dog 660) showed only a small patch of bronchopneumonia and marked emaciation from the long-standing obstruction with inadequate nutrition.

The clinical application of the evidence that has been presented that an important factor in death from high obstruction is the loss of the digestive secretions depends to a large extent on the individual case. Uncomplicated high obstruction does not occur frequently. The more usual picture is that of an obstruction lower in the intestinal tract or complicated by some necrosis of the bowel from strangulation or distention. Loss of digestive secretions occurs in varying degrees in the latter case, depending largely on the length of bowel above the obstruction that would afford an absorbing surface for the secretions. In many cases of this type toxemia may be the more important factor in causing death and may overshadow the rôle of the loss of digestive secretions, as suggested by Gatch and his co-workers.[1] The beneficial effect of the administration of saline probably depends on the degree to which the body has been depleted of fluid and blood electrolytes. This depletion is a much more outstanding feature in uncomplicated high obstruction than it is in low obstruction or occlusion with damage to the bowel. Hence the improvement following the administration of saline before surgical intervention would be expected to be in proportion to the importance of the factor of loss of digestive secretions. It is not likely that the saline appreciably influences the toxemia, and if

this is of importance in the particular case its beneficial effect in replacing the lost digestive secretions would probably be masked to some extent. It appears to us that the rational stand to take in regard to saline therapy is to advocate replacement of as much fluid and blood electrolytes as is reasonably possible before operation by large amounts of physiologic solution of sodium chloride or Ringer's solution given subcutaneously or intravenously when it appears that there has been a considerable loss of digestive secretions. Furthermore, any prolonged delay to permit extensive preoperative saline therapy does not seem justifiable, particularly because of the difficulty in determining the importance of the factor of toxemia and especially in predicting whether the obstruction is complicated by necrosis of the bowel, which would be benefited only by early operation and not by the saline. If the clinician is reasonably sure that the outstanding factor in a case of uncomplicated high obstruction is loss of digestive secretions, then resort to a more prolonged and extensive saline therapy before operation may be justified.

SUMMARY

When animals in which a high intestinal obstruction had been produced were treated by giving them about a liter daily of 1 per cent sodium chloride and from 5 to 7 per cent dextrose solution plus, in one instance, peptonized milk by a jejunostomy opening in the bowel below the obstruction, two survived fifty-two and seventy days, six others lived from seventeen to thirty-eight days, and thirty died between the second and fifteenth day. The animals that survived for the long periods showed no evidence of any so-called "toxic" symptoms. Vomiting occurred about every other day. Watery stools were sometimes passed when the dextrose was poorly tolerated, and occasionally a small solid stool. The weight showed a gradual decline, varying from a daily loss of 0.0771 to 0.195 Kg., or from 0.642 to 1.88 per cent of the original body weight. The total loss of weight was over half the original body weight for the animal that lived fifty-two days, and almost half for the animal that lived seventy days. Chemical studies of the blood showed that the chlorides remained at a normal level during the entire period of obstruction except in three instances, when the figures were much higher than normal. The carbon dioxide remained normal except in one instance, when it decreased on the day of death. The nonprotein nitrogen showed relatively little change, except an occasional slight rise. At autopsy the stomach and obstructed bowel were found to be moderately distended. There was a considerable thickening of the wall of the bowel just above the obstruction in animals that survived for long periods. The immediate cause of death was definitely due to a complication, either pulmonary or abdominal, in most

of the animals. In the two animals that survived fifty-two and seventy days, the outstanding feature was marked emaciation. In a series of four dogs with high intestinal obstruction, distilled water was administered through the jejunostomy opening. These animals died in five, six, eight and eleven days, without any postmortem changes other than the obstruction. Chemical analysis of the blood of the two dogs that lived eight and eleven days showed the usual changes of untreated animals with obstructions.

CONCLUSIONS

1. In high intestinal obstruction an important factor in the cause of death is the loss of digestive secretions. This view is supported by observations in this experiment in which some animals lived from fifty-two to seventy days with a high obstruction. The rôle of the sodium chloride solution, which was administered daily through a jejunostomy opening below the obstruction, was to replace the water and important blood electrolytes, fixed base (chiefly sodium) and chloride ions, which are ordinarily lost from failure of resorption and vomiting.

2. In regard to obstruction low in the intestinal tract or complicated by necrosis of the bowel, the loss of digestive secretions may be a factor in the cause of death, but this is of varying importance, depending on the length of bowel above the obstruction which would offer opportunity for some resorption of the secretions. It is in this group tha toxemia probably plays the more important rôle, and in man operative treatment should be resorted to immediately.

3. The beneficial effect of the administration (subcutaneously or intravenously) of saline solutions clinically in cases of intestinal obstruction appears to depend largely on the extent to which the body has suffered from the loss of digestive secretions from failure of resorption and vomiting. When toxemia is a conspicuous factor, its benefit may be masked to some extent.

ADDENDA

Since submitting this article for publication, we have kept an animal with a high intestinal obstruction alive for eighty days. This dog also was treated by the injection of a saline and dextrose solution into the bowel below the obstruction, but in addition intestinal contents obtained from an animal with an intestinal fistula were given. Autopsy showed bronchopneumonia.

Benedict, Stewart and Cutner [31] reported that they kept an animal with high obstruction alive for fifty-eight days by administering a liter or more of physiologic solution of sodium chloride daily in the bowel below the obstruction.

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BREAKING STRENGTH OF HEALING FRACTURED FIBULAE OF RATS

VI. OBSERVATIONS ON THE INFLUENCE OF BILATERAL OVARIECTOMY

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The ovaries of the female are concerned not only with the regenerative functions of the animal, but also to no small extent with its metabolism in general. The influence exerted by the ovaries on the growth and repair of bone is incompletely understood, and little work has been done on this aspect of the problem. For this reason we decided to determine the effect of bilateral ovariectomy on the breaking strength of fractured and unfractured fibulae of rats.

Marsiglia,[1] estimating the process of calcification in fractured bones by means of roentgenograms, was unable to demonstrate that extirpation of the ovaries influenced the formation of the callus. Reach [2] found a slight reduction in the calcium oxide content of the skeleton of mice following the removal of the ovaries, and Korenchevsky [3] was unable to find any essential difference by chemical or histologic examination in the skeletons of growing rats after ovariectomy. On the contrary, Poncet,[4] Selheim,[5] Pirsche [6] and Tschirvinsky [7] found that the growth of the epiphysis continued beyond the normal limits after castration. Selheim particularly demonstrated this effect in dogs. In

From the Department of Surgery, Yale University School of Medicine.
The expenses of this investigation were defrayed by Davis and Geck, Inc.

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osteomalacia, controversy has existed for a long time as to the beneficial results of ovariectomy. Fehling,[8] for one, showed that the disease was markedly benefited by the removal of the ovaries, and Goldthwait and his associates,[9] in an interesting case report, reported a positive calcium balance in a patient with osteomalacia following ovariectomy. It is, however, not to be forgotten that the interdependency of the glands of internal secretion make it extremely difficult, if not at present impossible, to attribute particular disease phenomena entirely to one gland.

PROCEDURE

Young female rats weighing from 150 to 190 Gm. were selected for study. After they were on a standard diet[10] for one week, a bilateral ovariectomy was performed on half of the forty animals used in the experiment. In all forty the right fibula was fractured by the method described before,[11] and the animals returned to their cages. On the ninth postoperative day five of the rats with ovariectomies, and five with fractured fibulae only, were killed. This procedure was repeated on the fifteenth, twenty-first, twenty-seventh and thirtieth postoperative days. Their fractured right and unfractured left fibulae were then prepared as described elsewhere,[11] and the breaking strengths determined. In addition, the relative body weights of the rats, the amounts of the ration they consumed and the roentgenographic appearance of their calluses at different days of healing were determined.

RESULTS

To avoid confusion, those rats with bilateral oophorectomies, as well as fractured right fibulae, have been designated the ovariectomy fractured group, while those with only fractured right fibulae, and without ovariectomies, are called the ovariectomy control group.

The Breaking Strengths of the Fibulae: For the Ovariectomy Fractured Group.—The breaking strength ratios, the details for the calculation of which have been given in a former paper,[11] were used throughout this study.

The fractured right fibulae in these animals had a ratio of 38 on the ninth day of healing. By the fifteenth day the ratio had risen slightly to 82, and on the twenty-first day it was 128. The highest point reached was gained on the twenty-seventh day, when a ratio of 207 was found. The ratio for the final and last observation on the thirtieth day was 143.

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11. McKeown, R. M.; Lindsay, M. K.; Harvey, S. C., and Howes, E. L.: The Breaking Strength of Healing Fractured Fibulae of Rats: II. Observations on a Standard Diet, Arch. Surg. **24**:458 (March) 1932.

The unfractured left fibulae began on the ninth day with a ratio of 165, which had increased to 241 by the fifteenth day, but thereafter fell on the twenty-first day to 193. The ratio on the twenty-seventh day was 299, and on the thirtieth day 255.

When the foregoing results were charted, it was seen that the healing strength of the fractured right fibula rose in almost a straight line to the twenty-seventh day. In earlier experiments we found that the strength of the callus increased to the fifteenth day, when the primary callus was considered to have been formed, and that from the fifteenth to the twenty-first day there was an abrupt loss in the healing strength, which was felt to be largely due to the rapid development of the medullary cavity at that time.[12] We found no such peak on the fifteenth day in the rats with bilateral oophorectomies, but did observe a peak on the twenty-seventh day. Nor did we note a secondary drop in strength in the callus between the fifteenth and twenty-first days as

TABLE 1.—*Breaking Force and Ratio of Fractured and Unfractured Fibulae of Ovariectomy Fractured Group* *

Postoperative Days	Ratio for Unfractured Left Fibulae	Ratio for Fractured Right Fibulae
9	165	38
15	241	82
21	193	128
27	299	207
30	255	143

* Refer to table 1a for complete data.

we had in former work. There was, however, a drop in the strength of the fracture in the ovariectomized animals after the twenty-seventh day, which we do not believe to be of the same significance as the secondary drop normally occurring earlier (fig. 1).

The strength of the unfractured left fibulae in this group of animals varied in a manner closely resembling that found to characterize the left fibulae on other diets.[12] Ordinarily we have come to expect that the strength of the left fibula rises and falls when the strength of the right fibula rises and falls. As the strength of the fracture increases, at first the strength of the unfractured left fibula has also been found to grow greater. The right naturally increases more rapidly, but both rise simultaneously. When the right normally loses strength between the fifteenth and twenty-first days, the left likewise diminishes, but in this case at a more rapid rate than the right. However, here we find the left showing independently the type of breaking

12. McKeown, R. M.; Lindsay, M. K.; Harvey, S. C., and Lumsden, R. W.: Breaking Strength of Healing Fractured Fibulae of Rats: III. Observations on a High Fat Diet, Arch. Surg. **25**:467 (Sept.) 1932.

strength curve we have come to expect, while the right, on the contrary, was seen to increase without variation until it reached the twenty-seventh day. Evidently the removal of the ovaries has more effect on the fractured than it does on the unfractured fibula.

For the Ovariectomy Control Group.—The fractured right fibulae in the control group had a breaking strength ratio on the ninth postoperative day of 77. On the fifteenth day the ratio had risen to a peak, such as was found elsewhere to be one normally occurring at that time,[11] and had a ratio of 155. The ratio thereafter fell, as it

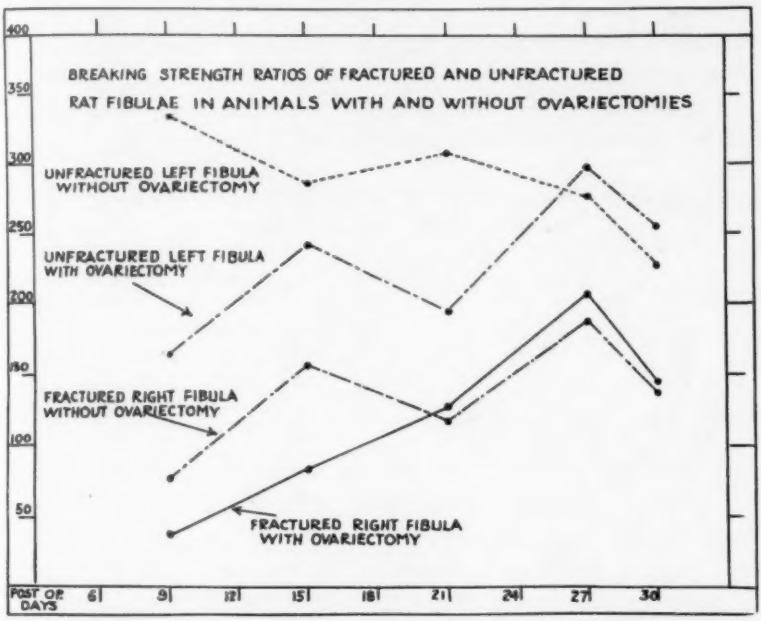

Fig. 1.—The ovariectomized rats showed a characteristic breaking strength curve for the left fibula. The right fibula was atypical, since the secondary drop in healing strength did not develop between the fifteenth and twenty-first days. The control rats with their ovaries intact showed a persistent reduction in the strength of their left fibula. That of the right fibula, however, rose and fell as we normally expect it to. Usually that of the left rises and falls simultaneously with the right. Consequently, we felt the metabolism of the control rats to be inadequate in maintaining the normal strength relationship between the two fibulae.

theoretically should, to 119 on the twenty-first day. On the twenty-seventh day it rose once more to reach a ratio of 189. At the last observation the ratio was 136.

The unfractured left fibulae in the controls began on the ninth day with a ratio of 333, which by the fifteenth day had fallen to 286. Thereafter it was found to be 309 on the twenty-first day, 278 on the twenty-seventh day and 239 on the thirtieth day (fig. 1).

The fractured right fibulae in the control group showed a closer resemblance to normal than did the fractured right fibulae of the ovariectomized rats. This was expected, as the control rats were ostensibly normal animals. The differences found between the fractured right fibulae of the control group in this paper, and the normal fractured right fibulae as established in a former contribution,[11] lie primarily in the height of the ratio attained. The character of the curves was the same for the two, but the control rats did not possess the strength of the normals.

The unfractured left fibulae in the control group did not resemble the normal as much as did the left fibulae of the ovariectomized rats. The changes in the fibular strength of the control left fibulae were not seen to take place simultaneously with rises and falls in the strength of its fractured right fibulae. On the contrary, the strength of the unfractured left fibulae in the control group fell throughout the experiment.

TABLE 2.—*Breaking Force and Ratio of Fractured and Unfractured Fibulae of Ovariectomy Control Group* *

Postoperative Days	Ratio for Unfractured Left Fibulae	Ratio for Fractured Right Fibulae
9	333	77
15	286	155
21	309	119
27	278	189
30	239	136

* Refer to table 2a for complete data.

We have already noted that the strength of the left fibulae in those animals with their ovaries removed fluctuated in a characteristic manner, but the plotted ratios in figure 1 show no such variations in strength for the control left fibulae. The explanation of this is apparently concerned in the metabolism of the control group. As will be shown later, the control rats lost weight consistently, and we have found elsewhere that the weight of the animal exerts a decided influence on the strength of its fibulae.[11]

Relative Studies on Animal Weights and Food Consumption: For the Ovariectomy Fractured Group.—The body weights of this group fell from the ninth to the twenty-first postoperative days, when they again became normal (table 3). Subsequently the weights decreased at a rapid rate to the twenty-seventh day, after which the previous loss was somewhat regained, and the final weighings on the thirtieth day were not greatly below normal (fig. 2).

The food consumed by the ovariectomized group remained relatively constant until the twenty-first day was reached, when a definite increase in the quantity of the diet ingested took place. Thereafter the quantity was about the same as that taken by the control rats (table 3 and fig. 2).

The weights of the ovariectomized rats were greater than those of the control group. This is in at least partial agreement with common opinion that an increase in body weight follows extirpation of the ovaries. Concomitantly, the quantity of food ingested by the oophorectomized animals was slightly more than that taken by the control rats.

For the Ovariectomy Control Group.—The body weights of this group were lower throughout than those of the ovariectomized animals, except for the twenty-seventh day when they were slightly higher (table 4). There is reason to believe that the metabolism of the control rats was insufficient to maintain the characteristic rise and fall in the

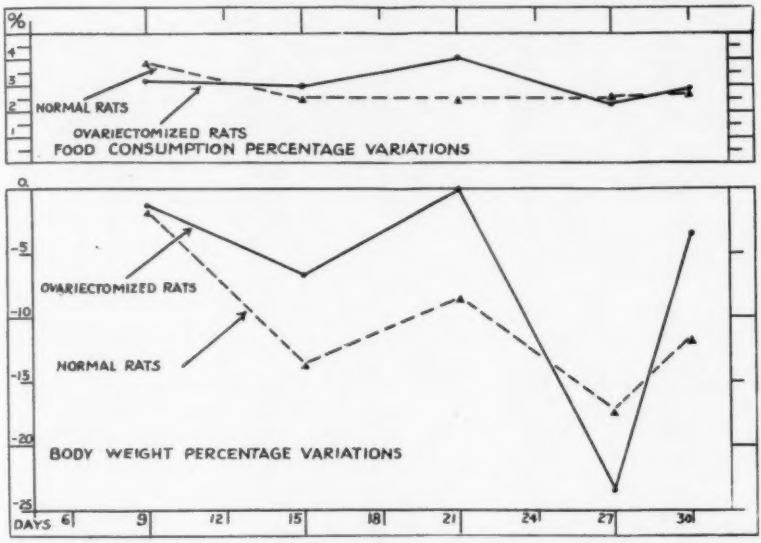

Fig. 2.—Body weight plotted as percentage difference in body weight from operation to death, and food consumption plotted as percentage body weight at operation.

strength of the unfractured left fibulae such as had been found to be the normal occurrence in unfractured left fibulae with animals in which be the normal occurrence in unfractured left fibula with animals in whom the right fibula was fractured.[11] This failure of the unfractured left fibulae in the control lot to approach the normal findings, despite the fact that the fractured right fibulae in the same group did resemble the normal fractured right fibulae, may mean that the metabolism was insufficient to prevent the fractured right from withdrawing from the unfractured left fibulae those elements of healing strength, probably largely calcium and phosphorus salts, which the metabolism of the rats was unable to furnish from the diet as it had been in the group formerly reported.[11]

The food consumed by the control rats was slightly less than that taken by the ovariectomized rats (table 4 and fig. 2). The difference was so little, however, that it was comparatively insignificant. Evidently, although the ovariectomized and control rats ate nearly the same amount of their ration, the ovariectomized group was better able to maintain weight than the controls. This may be further evidence of the abnormal metabolism of the controls, or on the other hand it may be but evidence of the reduced metabolism of the ovariectomized lot. The latter is probably the more likely of the two. However, when we compared the weights of the control group with those reported for the

TABLE 3.—*Summary of Body Weights and Food Consumption of Ovariectomy Fractured Group* *

Postoperative Days	Difference in Weight from Operation to Death as per Cent of Body Weight at Operation	Food Consumed per Day from Operation to Death as per Cent of Body Weight at Operation
9	— 0.6	3.2
15	— 6.3	3.0
21	0.0	4.1
27	—23.2	2.4
30	— 3.5	2.9

* Refer to table 3a for complete data.

TABLE 4.—*Summary of Body Weights and Food Consumption of Ovariectomy Control Group* *

Postoperative Days	Difference in Weight from Operation to Death as per Cent of Body Weight at Operation	Food Consumed per Day from Operation to Death as per Cent of Body Weight at Operation
9	— 1.7	3.9
15	—13.6	2.6
21	— 8.3	2.6
27	—17.1	2.6
30	—11.3	2.8

* Refer to table 4a for complete data.

standard diet group in a former paper [11] it was apparent at once that the weights of the controls, in the light of the earlier work, were not normal. In the standard diet group we had found body weight maintained above normal until the eighteenth day, with a slight drop below normal on the twenty-first day, and a point on the thirtieth day decidedly above the original weight at the onset of the experiment. Nothing resembling this was found on the weights of the ovariectomy controls. They fell from the beginning to the end of the study. Consequently, it is quite likely that these control rats were metabolically subnormal, which would account to no small extent for the variation from the normal found in their fibular breaking strength.

ROENTGENOGRAPHIC STUDIES OF REPRESENTATIVE FRACTURES

Of the Ovariectomized Rats.—The calcification of the callus in these fractures was observed to be retarded (fig. 3). The density of the callus was appreciably less on the ninth, fifteenth and twenty-first days than it was in the controls. A poorly selected roentgenogram of the twenty-seventh day control fracture made a comparison on that day

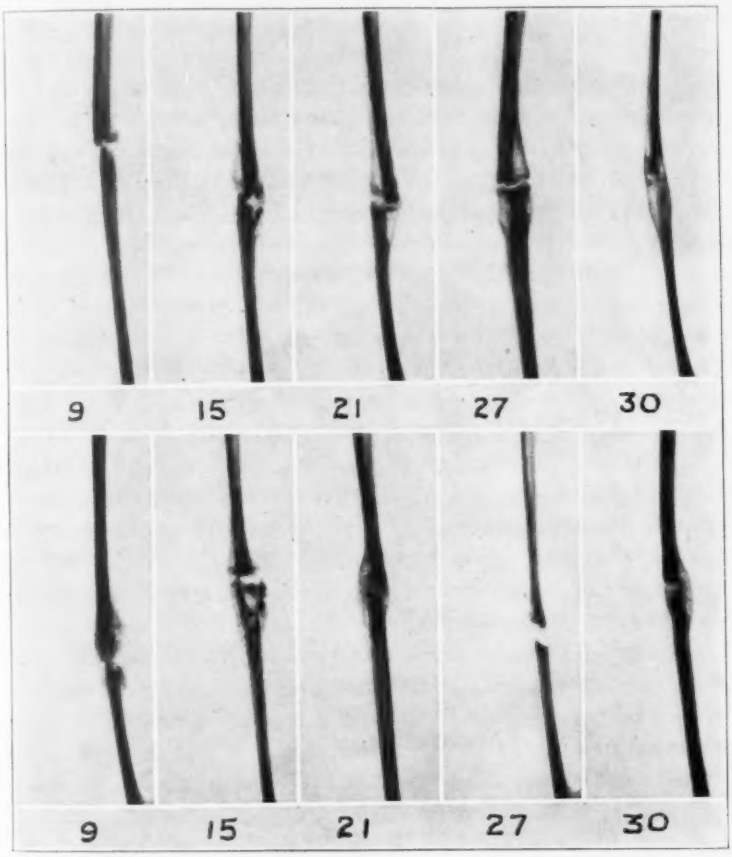

Fig. 3.—Representative roentgenograms at different postoperative intervals. The upper section of roentgenograms shows the fractured right fibulae of ovariectomized rats; the lower section, the fractured right fibulae of normal female rats. With the exception of the twenty-seventh day fracture, the controls appear to possesss more calcific material, and consequently more strength, than the calluses of the ovariectomized rats. Prior to the twenty-first day this evidently was true, but later it is questionable. Due to the lack of agreement between the roentgenograms and the breaking strengths, we have come to believe the roentgenogram an inadequate index of healing strength.

impossible. On the thirtieth day, however, the ovariectomized rat still showed less calcium deposited in its fracture than was noted in the control callus.

Of the Ovariectomy Controls.—Calcification of the healing fracture progressed at a normal rate in the ovariectomy controls (fig. 3). In that respect they so closely resembled the standard diet fracture series described before [11] that no attempt will be made to consider them further.

COMMENT

The healing strength of fractured fibulae of rats on whom bilateral oophorectomies had been performed was below that of their controls until the twenty-first day postoperatively. Subsequently the healing strength was slightly greater. By roentgenographic examination it appeared that in large part the early diminution in strength was due to a delay in the process of calcification of the primary callus. The delay may possibly have been due to the production of a negative calcium balance, which, however, is not in accord with the findings of others on osteomalacia where a positive calcium balance with an increase in the density of the bones of the body was said to have followed extirpation of the ovaries.[13] It is not to be forgotten that in cases of parathyroidectomy the calcium of the blood stream is increased, and yet it has not been satisfactorily demonstrated that fractures heal the quicker as a result of such an elevation. Evidently the form in which the calcium exists in the blood stream is of as much, if not more, importance than is a quantitative increase. Furthermore there is a question as to whether one may compare osteomalacia and a fracture in respect to their effects on calcium metabolism in rats.

The metabolism of ovariectomized rats is by far too large for us to attempt, or even to desire, to create the impression that removal of the ovaries in female rats will of itself slow up the healing of fractures by inhibiting the deposition of calcium salts. We shall show at a later date that orchidectomy, and possibly thyroidectomy, and parathyroidectomy will produce a similar reduction in the healing strength of fractured rat fibulae. The metabolism of the salts utilized in the repair of bone is so intimately bound up with many of the glands of internal secretion that as yet no particular one is definitely known to control the entire picture.

The body weights of the ovariectomized rats did not show an absolute gain. Rather one may say their weights were more completely maintained than were those of the controls, yet the weights were never greater than normal, or more correctly greater than the original weight

13. Fehling;[8] Goldthwait, Painter, Osgood and McCrudden.[9]

at the beginning of the experiment. The influence of castration has been investigated in the human female by Geist and Goldberger,[14] who found that at best a slight increase in body weight followed oophorectomy. At the same time there was a very moderate drop in the basal metabolic rate, while the blood chemistry changed but little, if at all. It would seem possible that in the ovariectomized rats the better maintenance of body weight might in part be explicable by a reduction in the metabolism along with a somewhat greater consumption of food.

CONCLUSION

Female albino rats with fractured right fibulae, and bilateral oophorectomies, had less strength in their healing callus for the first twenty-one days of healing than did their controls in which the ovaries were not removed, but which also had had their right fibulae fractured. Later the strength of the calluses in the ovariectomized rats was slightly greater than that of the control calluses.

The formation of the primary callus in ovariectomized rats during the first twenty-one days of the reparative process would seem to be more influenced than were the later stages in the repair of the fracture. The findings on the breaking strength machine were substantiated in part by similar findings on roentgenographic examination. Roentgenographic studies of selected fractures over the observed intervals strongly suggested a retardation in the calcification of the provisional callus.

The better maintenance of body weight in the ovariectomized group than in their controls was in agreement with similar findings by other workers.

ADDENDA

COMPLETE DATA ON OVARIECTOMIZED RATS

TABLE 1a.—*Breaking Strength and Ratio for Fractured Right and Unfractured Left Fibulae of Ovariectomy Fractured Group*

Postoperative Days	Rat No.	Weight (W)		Force (F)		Ratio (R)	
		Operation	$(10.W)^{2/3}$	Left	Right	Left	Right
9	3081	178	146.9	250	..	170	0
	3082	170	142.5	260	90	182	63
	3083	172	143.6	280	50	195	34
	3086	176	145.8	155	90	106	62
	3087	185	150.7	295	70	196	46
	3088	180	148.0	205	35	139	24
Arithmetic mean						165±13	38±9
15	3147	160	136.8	195	90	143	66
	3148	182	149.1	575	90	386	60
	3150	180	148.0	280	75	189	51
	3151	180	148.0	350	120	236	81
	3153	176	145.8	425	175	291	120
	3154	185	150.7	215	100	143	66
	3157	158	135.7	410	180	302	133
Arithmetic mean						241±32	82±11

14. Geist, S. H., and Goldberger, M. A.: Am. J. Obst. & Gynec. **12**:206, 1926.

TABLE 1a.—*Breaking Strength and Ratio for Fractured Right and Unfractured Left Fibulae of Ovariectomy Fractured Group—Continued*

Postoperative Days	Rat No.	Weight (W)		Force (F)		Ratio (R)	
		Operation	$(10.W)^{2/3}$	Left	Right	Left	Right
21	3163	162	137.9	250	245	181	178
	3164	172	143.6	325	200	226	139
	3165	180	148.0	210	85	142	57
	3166	154	133.4	305	140	229	105
	3167	152	132.2	245	215	185	163
Arithmetic mean						193±15	128±20
27	3379	150	131.0	355	335	271	256
	3380	160	136.8	420	295	307	216
	3381	162	137.9	355	225	257	163
	3383	142	126.3	415	275	329	218
	3384	160	136.8	455	250	333	183
Arithmetic mean						299±14	207±15
30	3527	185	150.7	360	125	239	83
	3622	170	142.5	505	210	354	147
	3623	172	143.6	350	275	244	192
	3624	170	142.5	350	275	246	193
	3625	150	131.0	330	230	252	176
	3626	180	148.0	290	95	196	64
Arithmetic mean						255±20	143±21

TABLE 2a.—*Breaking Strength and Ratio for Fractured Right and Unfractured Left Fibulae of Ovariectomy Control Group*

Postoperative Days	Rat No.	Weight (W)		Force (F)		Ratio (R)	
		Operation	$(10.W)^{2/3}$	Left	Right	Left	Right
9	3786	190	153.4	560	30	365	20
	3787	165	139.7	420	0	301	0
	3788	165	139.7	600	225	429	161
	3789	180	148.0	355	235	240	159
	3790	165	139.7	360	0	258	0
	3678	173	144.1	580	175	403	121
Arithmetic mean						333±29	77±30
15	3668	168	141.4	385	275	272	194
	3670	150	131.0	360	225	275	172
	3671	194	155.6	460	340	296	219
	3672	153	132.8	440	160	331	120
	3669	178	146.9	375	105	255	71
Arithmetic mean						286±12	155±24
21	3684	186	151.3	460	35	304	23
	3685	168	141.4	550	240	389	170
	3686	180	148.0	480	25	324	17
	3687	196	156.6	430	145	275	93
	3683	172	143.6	365	420	254	292
Arithmetic mean						309±21	119±47
27	3688	170	142.5	300	245	211	172
	3689	180	148.0	300	270	203	182
	3690	164	139.1	415	340	298	244
	3692	173	144.1	560	250	389	173
	3691	162	137.9	400	240	290	174
Arithmetic mean						278±31	189±13
30	3673	156	134.6	365	200	271	149
	3675	168	141.4	310	240	219	170
	3674	165	139.7	440	90	315	64
	2322	182	149.1	225	240	151	161
Arithmetic mean						239±31	136±21

TABLE 3a.—*Body Weights and Food Consumed by Rats of Ovariectomy Fractured Group*

Postoperative Days	Rat No.	Weight			Food Consumed	
		Start	Operation	Death	Start to Operation	Operation to Death
9	3081	175	178	180	60	60
	3082	180	170	165	40	40
	3083	170	172	164	61	39
	3086	186	176	180	53	50
	3087	180	185	192	54	60
	3088	175	180	172	61	53
Arithmetic mean		178	177	176	55	50
15	3147	176	166	168	55	92
	3148	185	182	148	42	67
	3150	175	180	168	58	76
	3151	180	180	174	50	84
	3153	180	176	128	44	37
	3154	185	185	180	53	111
	3157	170	158	180	34	86
Arithmetic mean		179	175	164	48	79
21	3163	166	162	146	46	111
	3164	170	172	194	78	174
	3165	174	180	178	65	153
	3166	153	154	158	53	168
	3167	152	152	142	46	107
Arithmetic mean		163	164	164	58	143
27	3379	139	150	102	52	94
	3380	169	160	116	26	101
	3381	162	162	134	35	100
	3383	140	142	110	42	95
	3384	170	160	132	41	114
Arithmetic mean		156	155	119	39	101
30	3527	176	185	194	42	173
	3622	168	170	165	53	131
	3623	165	172	140	55	120
	3624	178	170	176	70	125
	3625	162	150	140	38	121
	3626	180	180	172	48	213
Arithmetic mean		172	171	165	51	147

Summary

Postoperative Days	Weight at Operation, Gm.	Difference in Weight from Operation to Death, Gm.	Food Consumed per Day from Operation to Death, Gm.	Difference in Weight from Operation to Death as per Cent of Weight at Operation	Food Consumed per Day from Operation to Death as per Cent of Weight at Operation
9	177	— 1	5.6	— 0.6	3.2
15	175	—11	5.3	— 6.3	3.0
21	164	0	6.8	0	4.1
27	155	—36	3.7	—23.2	2.4
30	171	— 6	4.9	— 3.5	2.9

TABLE 4a.—*Body Weights and Food Consumed by Rats of Ovariectomy Control Group*

Postoperative Days	Rat No.	Weight			Food Consumed	
		Start	Operation	Death	Start to Operation	Operation to Death
9	3786	185	190	170	53	30
	3787	152	165	155	60	52
	3788	164	165	160	55	60
	3789	165	180	180	62	65
	3790	155	165	165	48	92
	3678	170	178	187	50	62
Arithmetic mean		165	178	170	55	60

TABLE 4a.—*Body Weights and Food Consumed by Rats of Ovariectomy Control Group—Continued*

Postoperative Days	Rat No.	Weight			Food Consumed	
		Start	Operation	Death	Start to Operation	Operation to Death
15	3668	158	168	152	57	75
	3670	150	150	140	46	61
	3671	175	194	180	66	89
	3672	158	153	120	46	30
	3669	150	178	140	65	73
Arithmetic mean.....		158	169	146	56	66
21	3684	168	186	185	62	121
	3685	160	168	160	45	87
	3686	182	180	165	48	85
	3687	180	196	175	62	118
	3683	158	172	140	66	72
Arithmetic mean.....		170	180	165	57	97
27	3688	164	170	142	40	120
	3689	180	180	140	40	133
	3690	165	164	150	54	136
	3692	165	173	145	57	118
	3691	156	162	130	47	115
Arithmetic mean.....		166	170	141	48	122
30	3673	155	156	135	53	157
	3675	170	168	140	54	105
	3674	170	165	140	38	125
	2322	182	182	182	74	182
Arithmetic mean.....		169	168	149	55	142

Summary

Postoperative Days	Weight at Operation, Gm.	Difference in Weight from Operation to Death, Gm.	Food Consumed per Day from Operation to Death, Gm.	Difference in Weight from Operation to Death as per Cent of Weight at Operation	Food Consumed per Day from Operation to Death as per Cent of Weight at Operation
0	173	— 3	6.7	— 1.7	3.9
15	169	—23	4.4	—13.6	2.6
21	180	—15	4.6	— 8.3	2.6
27	170	—29	4.5	—17.1	2.6
30	168	—19	4.7	—11.3	2.8

SYPHILIS OF THE STOMACH

WITH SPECIAL REFERENCE TO ITS RECOGNITION AT OPERATION

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AND

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Opinions regarding the incidence of syphilis of the stomach are extremely divergent. Judging from the number of cases reported in the past few years by roentgenologists and gastro-enterologists one would conclude that involvement of the stomach is not at all uncommon. For instance, LeWald [1] in 1923 recorded fifty cases examined by himself personally in which the radiologic diagnosis was gastric syphilis. Eusterman [2] in 1930 described observations on ninety-three patients in whom the diagnosis of syphilis of the stomach was made on clinical grounds. Many smaller series are reported by roentgenologists and clinicians both in this country and abroad. The relative frequency of syphilis of the stomach as determined clinically is in sharp contrast to its rarity based on postmortem statistics (see Konjetzny [3]). Pathologists in general are therefore inclined to look on most clinical reports as unreliable. Their attitude is tersely expressed in a statement by Sternberg [4] that merely the number of *reports,* not the number of *cases* of syphilis of the stomach, has increased.

In a previous publication dealing with the incidence of gastric syphilis we [5] upheld the clinician's point of view in contending that the disease was not particularly uncommon. We attempted to explain the

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From the Department of Surgery, Northwestern University Medical School; the Department of Medicine, University of Illinois College of Medicine, and the Cook County Hospital.

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4. Sternberg, C., quoted by Windholz, F.: Ueber erworbene Syphilis des Magens, Virchows Arch. f. path. Anat. **269**:384, 1928.

5. Singer, H. A., and Meyer, K. A.: Syphilis of the Stomach, with Special Reference to Its Incidence, Surg., Gynec. & Obst. **48**:23 (Jan.) 1929.

rarity with which the disease was seen by the morbid anatomist in the following manner: The suggestion was made and evidence submitted to show that generally at the time a patient with gastric syphilis reaches the autopsy table the lesion either has completely resolved or has lost its specific characteristics in undergoing transformation into scar tissue. According to this assumption, the pathologist encounters the disease usually in an unrecognizable form or in a stage in which the histologic characteristics are not classic. The clinician, on the other hand, is frequently afforded the opportunity of detecting the disease at the height of its activity and of watching its disappearance either spontaneously or following therapy. It is not to be inferred from the foregoing statements that we consider the disease to be a common one, and that we accept the diagnosis of gastric syphilis in most of the reported cases. As a matter of fact, we have been led to conclude that the number of nonsyphilitic cases mistaken for those of syphilis is greater than the number of specific cases overlooked (see Singer and Meyer [6]). The view that we entertain based on a combined clinical and pathologic study is that the disease is neither rare nor common. We believe that any surgeon who performs a considerable number of gastric operations should expect to encounter a syphilitic stomach from time to time but only at relatively long intervals.

The recognition of syphilis of the stomach at the operating table is of great importance, not alone for academic, but also for practical reasons. When the granulomatous infiltrate is sufficiently thick to be readily visible and palpable, the lesion is most commonly mistaken for carcinoma. The latter diagnosis indicates wide resection, a procedure that carries with it a mortality by no means negligible. Syphilitic involvement, on the other hand, generally requires no surgical procedure with regard to the stomach other than removal of tissue for biopsy. When an obstruction is present, gastro-enterostomy suffices. Resection is seldom required. The importance of avoiding extensive operations in gastric syphilis is emphasized by the frequent inability of wounds to heal in the presence of active syphilis. In cases in which the granulomatous infiltrate is relatively thin, the lesion can easily be overlooked, as will be shown later, unless the surgeon is acquainted with the specific anatomic characteristics. The failure to recognize the presence of a lesion of this type causes the surgeon to refrain from performing a gastro-enterostomy that might be indicated (see Larimore,[7] case 3).

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6. Singer, H. A., and Meyer, K. A.: Syphilis of the Stomach, with Special Reference to Its Misdiagnosis, Am. J. Surg., to be published.

7. Larimore, J. W.: Syphilis of the Stomach, Surg., Gynec. & Obst. **37**:133 (Aug.) 1923.

It tends also to mislead the gastro-enterologist, who may then assume that the condition is functional and therefore omit anti-syphilitic treatment.

The question naturally arises are the changes in syphilis of the stomach sufficiently distinctive to permit its recognition at laparotomy? We have been impressed, in recollecting our own cases and those reported in the literature or described to us by our colleagues, by the relative ease with which gastric syphilis in general is distinguished from ulcer or carcinoma. It is the exception rather than the rule for a surgeon who has had a fair amount of experience in gastric work to fail to recognize that he is dealing with an atypical type of lesion when he encounters syphilis of the stomach. For instance, LeWald [8] in discussing one of his cases reported from the radiologic standpoint stated, "The surgeon, on inspection and palpation of the growth, immediately said that he was convinced that the lesion was not due to carcinoma or to ulcer of the stomach and did not perform resection." If the operator has dealt with a similar case previously and learned that it was syphilitic, he generally suspects the diagnosis in the second case almost at once. Experience with a few cases is sufficient to permit the surgeon to make the diagnosis with a fair degree of confidence. Even without this experience, a theoretical knowledge of the gross characteristics of syphilis of the stomach generally leads to its identification. A frozen section of tissue taken for biopsy, as will be shown, is of little value in the diagnosis as compared with the gross examination.

Although numerous articles on gastric syphilis have appeared in surgical journals, none, so far as we have been able to ascertain, has dealt at any length with the gross features of the disease. Since at operation the lesion is recognized mainly by its macroscopic characteristics, it is deemed advisable to summarize the morphologic changes that serve to distinguish gastric syphilis from other gastric conditions. In the following paragraphs only those structures that are available for direct examination through an upper abdominal incision will be discussed. The presence of associated lesions elsewhere which are of aid in diagnosis, but which do not lend themselves to inspection at laparotomy, for instance an aneurysm of the thoracic aorta as recorded by Windholz,[9] will receive no special consideration.

It is to be borne in mind that the description which follows applies to the general run of cases, and that variations occur depending on the location, extent and stage of development of the granulomatous involvement. The lesion is most frequently found in the pars pylorica, often

8. LeWald, L. T.: Roentgen Diagnosis of Gastric Syphilis, J. A. M. A. **96**:179 (Jan. 17) 1931.

9. Windholz, F.: Ueber erworbene Syphilis des Magens, Virchows Arch. f. path. Anat. **269**:384, 1928.

producing obstruction to the gastric outlet. Less frequently, the process is located in the pars media. Involvement of the pars cardiaca is uncommon. Multiple localizations, especially in the pyloric and midportions of the stomach, are not rare. Separate lesions of the cardiac and middle thirds of the stomach as reported by Bensaude, Mezard and Godard [10] are relatively unique. The extent of the lesion varies between wide limits. The granuloma may be restricted to any of the three portions of the stomach mentioned, but also may involve any two or all three. A general involvement of the stomach is rare. Not infrequently, however, the middle and distal thirds of the stomach are simultaneously affected. Early in the disease, the lesion consists of a local, plaquelike infiltrate, which merely imparts a sense of thickening to the palpating hand. A lesion of considerable extent and thickness represents a further stage and is likely to be accompanied by secondary ulceration. Contraction of a segment, usually represented by a concentric, cylindric narrowing, is indicative of a late stage. Diffuse involvement of the stomach is followed by microgastria or leather-bottle stomach. It is to be remembered that up to a certain stage in its development the process is reversible. A thickened, rigid tube encountered at a primary laparotomy may, following specific treatment, as related by Le Noir,[11] be found supple, pliable, normally thin and patent at a subsequent operation.

In considering first the stomach itself, one is struck by the discrepancy in many cases between the radiologic and the anatomic changes. The x-ray picture may suggest the presence of an extensive lesion, whereas at operation one is surprised to see and feel but little anatomic alteration. Schlesinger [12] also mentioned that at laparotomy palpation may fail to disclose an abnormality, although the x-ray picture may reveal considerable deformity. The presence of pyloric stenosis was shown roentgenologically in a case reported by Eisenklam [13] and examined in Holzknecht's institute, which failed to show any anatomic narrowing at operation. A similar case examined by two qualified radiologists was reported by Petit-Dutaillis and Bertrand.[14] In the

10. Bensaude, R.; Mezard, J., and Godard, P.: Sur un cas de syphilis gastrique suivi pendant 20 ans, Arch. d. mal. de l'app. digestif **20**:1178 (Dec.) 1930.

11. LeNoir, P.: Syphilis et ulcére gastro-duodenal, Arch. d. mal. de l'app. digestif **20**:470 (April) 1930.

12. Schlesinger, H.: Die Magensyphilis, Klin. Wchnschr. **9**:171 (Jan. 25) 1930.

13. Eisenklam, I.: Ueber diffuse luetische Infiltration des Magens, Wien. klin. Wchnschr. **39**:182 (Feb. 11) 1926.

14. Petit-Dutaillis, D., and Bertrand, I.: Un cas curieux de syphilis gastrique grave sans tumeur, simulant le cancer. Vérification biopique. Gastro-entérostomie combinée au traitement spécifique. Guérison, Arch. d. mal. de l'app. digestif **20**: 199 (Feb.) 1930.

paucity of anatomic as compared with radiologic changes, gastric syphilis is in contrast to carcinoma, in which unfortunately the lesion is generally much more extensive than anticipated from its appearance in the x-ray picture.

The characteristic lesion of syphilis is a flat, plaquelike infiltrate that involves the submucosa principally. The most distinctive feature of this infiltrate is its relatively soft consistency. When the infiltrate is thin, it may be entirely overlooked, because it fails to impart the expected increased sense of resistance detected in carcinoma or ulcer. The softness combined with the flatness of the infiltrate readily leads to an oversight. Windholz [9] described a pertinent case of a woman of 36 who was subjected to an operation for what was interpreted roentgenologically as a new growth of the cardiac portion of the stomach. At operation no gastric lesion was detected, and the abdominal incision was closed. Later examination with a barium meal showed an extension of the process, and a second operation was undertaken. This time tissue for biopsy was removed, and histologic changes suggestive of syphilis were found. Gradual decrease in the size of the stomach in spite of antisyphilitic treatment later necessitated a gastrostomy. The patient died about one year after the original operation with typical subtotal linitis plastica of syphilitic nature. The radiologic aspects of the case were described by Schwarz [15] in a separate communication. Petit-Dutaillis and Bertrand [14] related that in a patient in whom gastric syphilis was encountered at operation they were unable to detect any noteworthy change in the wall of the stomach before incising it. Palpation gave at most the impression that the pylorus was a little thickened and indurated. The x-ray picture showed what was interpreted as linitis plastica of the pyloric portion of the stomach. The tissue for biopsy removed from the region chosen for a gastro-enterostomy stoma showed microscopically that the infiltration had extended far beyond the pars pylorica. A similar case (no. 3) was reported from the roentgen standpoint by Larimore.[7] The x-ray picture showed an annular defect of the pyloric portion of the stomach producing high grade obstruction. At the operation, no gastric lesion was identified by the surgeon. In the first of the two cases to be described in this paper, only a portion of the infiltrate beyond the pylorus was detected by the surgeon at the operating table.

When the infiltrate leads to noteworthy thickening of the wall of the stomach, the presence of a lesion is, of course, readily recognized. Its relatively soft consistency and its plaquelike form, however, serve to distinguish it from carcinoma and from the inflammatory tumor that

15. Schwarz, G.: Die Entwicklung eines syphilitischen Schrumpfmagens im Röntgenbilde beobachtet, Fortschr. a. d. Geb. d. Röntgenstrahlen **37**:313, 1928.

frequently accompanies ulcer. Except in leather-bottle types with marked shrinkage, the gastric wall is pliable and is only moderately increased in consistency as compared with the normal. The consistency of the infiltrate is fairly uniform, except at its margins, where it merges almost imperceptibly into the surrounding normal gastric wall. The degree of thickening varies between wide limits. However, irrespective of the amount of thickening, the point of maximum increase is in the center of the lesion, and the transition from the normal to the abnormal is a very gradual one. The great majority of lesions reported in the literature as well as in our own series answer to the foregoing description.

In addition to the characteristics described as determined by palpation, there are a few features noted on inspection which, although less distinctive, merit description. The peritoneum over the involved area is thickened, lusterless, opaque and often edematous. Aoyama [16] stated that he suspected the fourth case in his series of being syphilitic by the appearance of the exterior of the stomach. He noted more or less widespread whitish thickening, edematous swelling and focal injection. Occasionally, the surface of the stomach is reddened as in the case reported by Eisenklam.[13] However, this is not typical and is apparently due to secondary infection. Adhesions are generally absent, but may be prominent as in the second case to be described later.

Incision into the stomach often yields valuable information. If the wall is incised in the area of infiltration, i. e., for the purposes of a biopsy, the cross-section of the stomach will show the individual coats to be distinct. Extensions from the mucosa into the subjacent layers as in carcinoma are lacking. The thickening of the wall of the stomach is seen to be due to an increase chiefly of the submucosa, which is rendered homogeneous and edematous. The tissue here has fibrous rather than neoplastic characteristics. Exposure of the interior surface of the lesion by an opening made beyond the margin of infiltration often discloses more or less ulceration. The ulcers are frequently multiple and are irregular in shape with serpiginous outlines. The edges are only slightly raised and are not undermined. The floor of an ulcer is generally covered by a lardaceous membrane, which is lightly adherent. The ulcers are superficial, the floor being generally formed by the underlying thickened submucosa. The base of the ulcer is generally in the same niveau as the margins and projects above the level of the normal mucosa. The ulceration occupies the thickest portion of the granuloma, and thereby furnishes the impression that the denudation is secondary to the infiltration. Although superficial, the ulcers tend to

16. Aoyama, T.: Ueber syphilitische Erkrankung des Magens, Deutsche Ztschr. f. Chir. **174**:34, 1922.

be large, often reaching the size of the palm of a hand or larger (see fig. 2). Occasionally one finds extensive ulceration within which one or more islands of remaining mucosa are found (McNee,[17] Singer and Meyer [5] [case 2], Sparman [18]).

Of great assistance in the diagnosis at laparotomy are certain associated changes of syphilitic nature occurring particularly in the liver and the small intestine. The most frequent syphilitic lesion encountered in the abdomen is hepatic. The high incidence of syphilis of the liver in association with cases of gastric syphilis has been emphasized by Schlesinger.[12] Multiple deep stellate scars producing a classic hepar lobatum as occurred in the cases of Derman and Kopelowitsch [19] and Petit-Dutaillis and Bertrand [14] should immediately arouse the suspicion of syphilis when a gastric lesion co-exists. Less typical changes, such as limited scarring involving especially the left lobe and the region of the suspensory ligament as recorded by Windholz,[9] in his case 2, are also suggestive. Cicatrices limited to the right lobe, especially when superficial as in case 1 reported here, are of less significance. Practically complete shrinkage of the left lobe and involvement in the region of the attachment of the round ligament, with compensatory hypertrophy of the right lobe, are almost pathognomonic of syphilis of the liver. This type of lesion was found in Brams' [20] classic case of gastric syphilis. A similar hepatic involvement was encountered by Kwartin and Heyd [21] in their third case. Actual gummas, as might be expected, are less frequently encountered than scars. The presence of nodules in the liver may suggest carcinoma. The coexistence of gummas and scars as in one of our previous cases (Singer and Meyer [5]) should serve to identify the syphilitic nature of the nodules. A specimen for biopsy taken from one of the hepatic tumors as in case 4 of Downes and LeWald [22] would likewise aid in the diagnosis. The coincidence of syphilis of the liver and carcinoma of the stomach as mentioned by Gatewood and Kolodny [23] is constantly to be borne in mind by the

17. McNee, J. W.: Syphilis of the Stomach, Quart. J. Med. **15**:215, 1921-1922.

18. Sparman, R.: Ein Fall von Magen-Dünndarmsyphilis, zugleich ein Beitrag zur Kenntnis syphilitischer Magen-Darmerkrankungen, mit besonderer Berücksichtigung gummöser Veränderungen am Magen, Deutsche Ztschr. f. Chir. **164**: 136, 1921.

19. Derman, G. L., and Kopelowitsch, M. A.: Zur pathologischen Anatomie der syphilitischen Magengeschwüre, Virchows Arch. f. path. Anat. **278**:149, 1930.

20. Brams, W. A.: Ueber das Ulcus syphiliticum multiforme ventriculi, Arch. f. Verdauungskr. **27**:375, 1921.

21. Kwartin, B., and Heyd, C. G.: Syphilitic Ulcerations of the Stomach, Arch. Surg. **14**:566 (Feb.) 1927.

22. Downes, W. A., and LeWald, L. T.: Syphilis of the Stomach: A Report of Eight Cases with Roentgenologic Findings, J. A. M. A. **64**:1824 (May 29) 1915.

23. Gatewood, W. E., and Kolodny, A.: Gastric and Intestinal Syphilis: Report of a Case; Clinical Course and Morbid Pathology, Am. J. Syph. **7**:649 (Oct.) 1923.

surgeon. Syphilitic lesions involving the small intestine and the spleen are less common and less easily identified. The lesions of the small intestine tend to be multiple. Fraenkel's [24] case is a prototype of the gastro-intestinal form. Splenomegaly, according to Schlesinger,[25] is present only exceptionally. However, its detection should lead to a search for a cause.

Syphilitic lesions of the stomach often require laparotomy. The obstructive lesions of irreversible character and acute perforation obviously demand surgical intervention. However, aside from the vital indications, operation is frequently essential for identification of the lesion. The diagnosis of gastric syphilis is difficult in many cases principally on account of the close resemblance it bears to carcinoma. A filling defect in the stomach even in the presence of a positive Wassermann reaction, on the basis of statistics, is more likely to represent a malignant than a syphilitic process (Singer and Meyer [6]). The frequency of gastric carcinoma and the high incidence of constitutional syphilis render the diagnosis of gastric syphilis a hazardous one. On this account, Baumecker [26] considered laparotomy imperative. Although the therapeutic test can be invoked to aid in the determination of the nature of the lesion, there are certain limitations and disadvantages to this procedure. Although opinions differ somewhat regarding the length of time of trial, it is generally agreed that only a relatively short period is warranted. Stokes [27] advised in questionable cases the preoperative administration of two injections of arsphenamine, 0.3 Gm. each, with a three day interval. If improvement within seven days is not pronounced, and if the operability of the patient may be decreased by further delay, an exploration should be performed. Sinakevitch and Toporkoff [28] suggested treatment for from ten to fifteen days. Einhorn [29] recommended a test period of from two to four weeks or longer. Bockus and Bank [30] stated that Eusterman believed that six weeks is adequate to test the effect of antisyphilitic treatment.

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24. Fraenkel, E.: Zur Lehre von der acquirirten Magen-Darmsyphilis, Virchows Arch. f. path. Anat. **155**:507, 1899.

25. Schlesinger, H.: Syphilis und innere Medizin, Vienna, Julius Springer, 1926, pt. 2, p. 121.

26. Baumecker, H.: Die klinische Diagnose der hypertrophischen Magenlues, Med. Klin. **26**:1557 (Oct. 17) 1930.

27. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1927, p. 734.

28. Sinakevitch, N. A., and Toporkoff, N. N.: Syphilis of the Stomach from the Viewpoint of Surgery and Neuropathology, Vestnik khir. **21**:3, 1930.

29. Einhorn, M.: Syphilom des Magens. Heilung durch antiluetische Kur, Deutsche med. Wchnschr. **55**:1877 (Nov. 8) 1929.

30. Bockus, H L., and Bank, J.: Upper Gastrointestinal Disease Associated with Syphilis, Am. J. Syph. **13**:30, 1929.

The value of the therapeutic test is limited, whether it is applied for one or for six weeks, since a fair proportion of syphilitic patients fail to show appreciable improvement. For example, in case 2 of LeWald,[8] after five weeks of treatment the degree of improvement was so slight that resort to exploratory operation was deemed advisable. The lesion at operation was shown to be syphilitic. In case 7 of the series published by Bockus and Bank,[30] six months of intensive treatment was necessary before improvement became noticeable. We among others have had similar experiences. Another disadvantage of the therapeutic test is that at times it is misleading. For example, a patient with gastric carcinoma and constitutional syphilis may improve temporarily as a result of antisyphilitic treatment. This observation is attested to by O'Leary.[31] Stokes [27] mentioned a case of carcinoma in which sufficiently marked improvement was obtained to lead to the temporary diagnosis of syphilis, which was later reversed by the disclosure at operation when the patient finally began to decline again. We have had similar experiences (Singer and Meyer [6]). The most serious objection to the therapeutic test, however, is the time lost in the event that the lesion proves to be carcinomatous. The local extension of the neoplasm may not be as significant as its constitutional effect, which decreases the patient's vitality and renders him a poorer surgical risk. The seriousness of overlooking a carcinoma and the relative innocuousness of a laparotomy in the presence of gastric syphilis have led not only surgeons but also internists and syphilologists (see Gäbert,[32] Schlesinger,[12] Stokes [27] and Strauss [33]) to recommend surgical intervention, unless otherwise contraindicated, whenever the slightest suspicion of carcinoma is entertained.

In the recognition of gastric syphilis the surgeon cannot depend on the standpoint of positive diagnosis. Unlike carcinoma or sarcoma unlike one in carcinoma, for instance, is of limited value, at least from the standpoint of positive diagnosis. Unlike carcinoma or sarcoma, gastric syphilis presents no pathognomonic histologic changes. As pointed out in a previous publication (Singer and Dyas [34]), the specific lesion of syphilis, i. e., the gumma, as found, for instance, in the liver, has not been described in the stomach. The histologic diagnosis is based on the recognition of several characteristics occurring in combination rather than on any one specific feature. The demonstration of these

31. O'Leary, P. A.: Gastric Syphilis: Data Accumulated from 89 Cases, Am. J. Surg. **11**:286 (Feb.) 1931.

32. Gäbert, E.: Zur Kenntnis und Diagnose der Magensyphilis, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **40**:224, 1927-1928.

33. Strauss, H.: Ueber Magen-Syphilis, Med. Klin. **27**:275 (Feb. 20) 1931.

34. Singer, H. A., and Dyas, F. G.: Syphilis of the Stomach, with Special Reference to Certain Diagnostic Criteria, Arch. Int. Med. **42**:718 (Nov.) 1928.

characteristics usually requires sections from several areas and also special stains. A single section rapidly prepared and stained with hematoxylin and eosin or polychrome stains during the course of an operation generally fails to yield information that will permit even a presumptive diagnosis of syphilis. In actual practice, tissue for biopsy is generally removed from the margin of the lesion because of the difficulty in suturing the defect if the center of the lesion is chosen. Generally, the histologic changes at the periphery of the syphilitic infiltrate are at the most only suggestive of a specific infection. This statement is borne out by the experience of Windholz,[9] in whose second case the tissue for biopsy removed at operation failed to show the typical changes that were later demonstrated in the central portions of the lesion at autopsy. The greatest value of a biopsy in syphilis of the stomach lies in its negative worth, i. e., in excluding carcinoma, provided, of course, the section chosen is representative of the lesion present.

Even if biopsy material is obtained from several areas and the preparations are stained by various methods, the information derived from the microscopic study alone is often insufficient on which to base a diagnosis. Some of the most expert histopathologists (Fraenkel,[24] Erdheim [Sparman's[18] case]) require the presence of certain gross features before concluding that a lesion is syphilitic, even though the microscopic changes are typical. In the cases of Mühlmann,[35] and Gosset et al.,[36] the histologic examination proved of limited worth in the identification of the lesion, as compared with the gross appearance. Eusterman[2] in speaking of the patients in his series who were operated on, stated, "Resected specimens were obtained in 14 clinically authentic or probable cases. Biopsy specimens, several of them unsatisfactory, were obtained in five others." The inference to be drawn is that the biopsies failed to show microscopic changes that were as distinctive of syphilis as the clinical and gross anatomic characteristics. Our own observation has been that the more experience one acquires with syphilis of the stomach the more weight does one place on the macroscopic features in arriving at a diagnosis. In the last three cases that came under our observation we were able to make the diagnosis with confidence from the gross character of the lesion. The tissue taken for biopsy in each instance was reported by a competent pathologist as showing chronic, nonspecific inflammation. In the second case recorded here, the diagnosis of syphilis is not justified by the histologic appearance of the

35. Mühlmann, E.: Beiträge zum Schrumpfmagen auf luetischer Basis, Deutsche med. Wchnshr. **41**:733 (June 17) 1915.

36. Gosset, A.; Guttman, R. A., and Bertrand, I.: Syphilis gastrique infiltrée à forme tumorale. Résection. Examen histologique, Arch. d. mal. de l'app. digestif **20**:714 (June) 1930.

tissue taken for biopsy, yet the other available data, viz., the presence of syphilis, the therapeutic response, the subsequent course and especially the macroscopic nature, establish the diagnosis almost beyond any question of doubt.

We disagree with Kwartin and Heyd,[21] who contended that final judgment should rest on the microscopic changes, and that the macroscopic picture cannot be accepted as sufficiently clearcut to permit even a preliminary diagnosis. These authors report three cases all with macroscopic features generally considered characteristic of syphilis. In the first case, the histologic examination confirmed the gross diagnosis. In the second case, however, the microscopic diagnosis of tuberculosis was favored, and in the third a nonspecific etiology was assumed. Without attempting to enter into polemics, we wish to point out our reasons for believing that these authors have fallen into error by placing most emphasis on the histologic picture. In their case 2, the lesions described as histologically characteristic of tuberculosis are not at all unlike miliary gummas seen in syphilis of the stomach and other structures. Practically identical lesions were described by Fraenkel [24] in the lymph nodes, as well as in the gastro-intestinal tract, in his case of gastric syphilis, in which the diagnosis was almost unequivocally established. The "periarterial, endarterial and panphlebitic changes" such as were recorded by Kwartin and Heyd [21] in this second case are more likely to be syphilitic than tuberculous in origin. The absence of tubercle bacilli in histologic preparations likewise throws doubt on their diagnosis of tuberculosis of the stomach. In case 3 of Kwartin and Heyd again, we are inclined to look on the gross diagnosis as correct, although the microscopic appearance is not characteristic of syphilis. Hepatic involvement near the round ligament and absence of the left lobe of the liver, which were found in their third case, are pathognomonic of hepatic syphilis. The history of a positive Wassermann reaction in the husband's blood is also confirmatory evidence, especially since the blood of the patient was not tested. The lack of histologic changes typical of syphilis should not in this case be the decisive factor in arriving at a diagnosis. As has been shown in a previous publication (Singer [37]), in certain stages of the disease the lesions are likely to lose their specific microscopic characteristics in the stomach as they do, for instance, in the liver and rectum. It should be stated that Kwartin and Heyd are aware of many of these considerations and readily admit the difficulties in connection with the microscopic diagnosis of syphilis.

The two cases to be described now are particularly instructive from the standpoint of recognition of gastric syphilis at the operating table.

37. Singer, H. A.: Syphilis of the Stomach, with Special Reference to Its Relationship to Linitis Plastica, Am. J. Syph. **13**:391 (July) 1929.

REPORT OF CASES

CASE 1.—R. M., a colored woman, aged 36, was sent to the Cook County Hospital on July 22, 1931, from one of the local dispensaries with the diagnosis of pulmonary tuberculosis. The basis of the diagnosis made by the dispensary physician was apparently the extreme degree of emaciation, for the patient offered neither subjective nor objective evidence of intrathoracic abnormality. It was soon apparent to the house physician in the tuberculosis division that the cause of the patient's emaciation was an abdominal condition. On this account, roentgen exam-

Fig. 1 (case 1).—Roentgenogram showing a spigot-shaped deformity of the prepyloric portion of the stomach due to syphilis.

ination (fig. 1) with a barium meal was requested and the report made on July 23, 1931, was: "Annular constricting deformity of the pyloric portion of the stomach indicative of malignancy." The patient was thereupon transferred to the medical service with the diagnosis of pyloric obstruction.

In the medical ward, it was ascertained that the patient began to experience epigastric pain three years prior to admission. Vomiting and loss of weight accompanied the pain. Because of these symptoms she was operated on elsewhere, but was not clear regarding either the nature of the lesion found or the procedure instituted. Following the laparotomy, the vomiting subsided, but only for a short period. The other symptoms were uninfluenced. The pain, which involved the

epigastrium rather diffusely, was described as cramplike and persisted more or less constantly. Neither soda nor emesis afforded relief. During the three years of her illness, the patient had lost 122 pounds (55.3 Kg.), her present weight being 88 pounds (39.9 Kg.). No hematemesis had been noted. Physically, the essential changes included evidence of moderate anemia, extreme emaciation and debility. The pulse was rapid (120) and weak. The blood pressure was 90 systolic and 60 diastolic. Abdominal examination disclosed, in addition to the healed midline scar of the laparotomy, the outline of the stomach projecting above the level of the remainder of the abdomen. No visible peristalsis was observed, and no mass was palpated. On the dorsa of both hands were evidences of dermatitis. The diagnosis of pyloric carcinoma with symptomatic pellagra was made, and the condition of the patient considered terminal. The extreme dehydration and debility, it was thought, precluded the possibility of successful intervention at that time. Fluids were administered by intravenous and subcutaneous routes, following which the giving of liquids by mouth was attempted. Although some vomiting occurred, a fair proportion of the ingested material was retained. No diagnosis other than that of carcinoma was entertained until Sept. 7, 1931, when hematemesis associated with a series of tarry stools appeared. The possibility of a benign gastric ulcer loomed into prominence, and a more optimistic attitude was assumed. The patient was prepared for surgical intervention and operated on on Sept. 9, 1931, at 8 a. m.

The surgeon who performed the operation found the stomach to be somewhat decreased in size. There were adhesions that bound the stomach posteriorly and were particularly marked along the lesser curvature. The serosa was edematous and opaque. The pyloric portion of the stomach was thickened and tubular, but only slightly increased in consistency. The thickening was not limited to the tubular pyloric portion, but extended in the form of a plaque to involve the pars media, which was also relatively soft. The patient's condition was considered too poor to withstand a gastro-enterostomy. However, the surgeon removed a block of tissue from the wall of the stomach for biopsy and closed the laparotomy wound. The patient was returned from the operating room with an extremely rapid and thready pulse. The operating surgeon believed he was dealing with a sarcoma of the stomach, and at the conclusion of the laparotomy sought our opinions. From the surgeon's description of the character of the gastric lesion we immediately suggested the diagnosis of syphilis. No time was lost in examining the x-ray plates, which we felt lent support to our impression. We then attempted to interview the patient, who, although conscious, was too weak to furnish complete and trustworthy information regarding her past. We did learn, however, that she had married at the age of 14 and had had one miscarriage and no children. She denied knowledge of venereal disease. As a Wassermann test had not been performed, we ordered blood drawn for this purpose. The patient became progressively weaker and died at 6: 50 p. m., ten hours following operation. The next morning an autopsy was performed, and later in the day the result of the Wassermann test on the blood was reported four plus, and that of the Kahn test two plus.

Anatomic Diagnosis.—The postmortem examination was made twenty hours after death by Dr. R. H. Jaffé, whose anatomic diagnosis reads: "Ulcerative syphilitic gastritis; adhesions and stellate scars of the right lobe of the liver; aspiration pneumonia and abscess in the right upper pulmonary lobe; aspiration pneumonia in the left upper lobe; acinous tuberculosis of the right upper pulmonary lobe; brown atrophy and anemia of the liver; brown atrophy of the heart

and serous atrophy of the subepicardial fat; anemia of the kidneys; adhesions of the base of the right pulmonary lobe; adhesions of both tubes and ovaries; cholesteatosis of the gallbladder; marked emaciation; recent and ancient laparotomy wounds; pellagra-like changes of the skin of the hands."

Gross Appearance of Stomach (Fig. 2).—The unopened stomach was filled with preserving fluid for museum purposes and its interior examined after fixation by removal of a portion of the anterior wall.

The stomach had an anomalous form, the proximal two thirds being globular, the distal one third cylindric. The globular portion consisted of the moderately

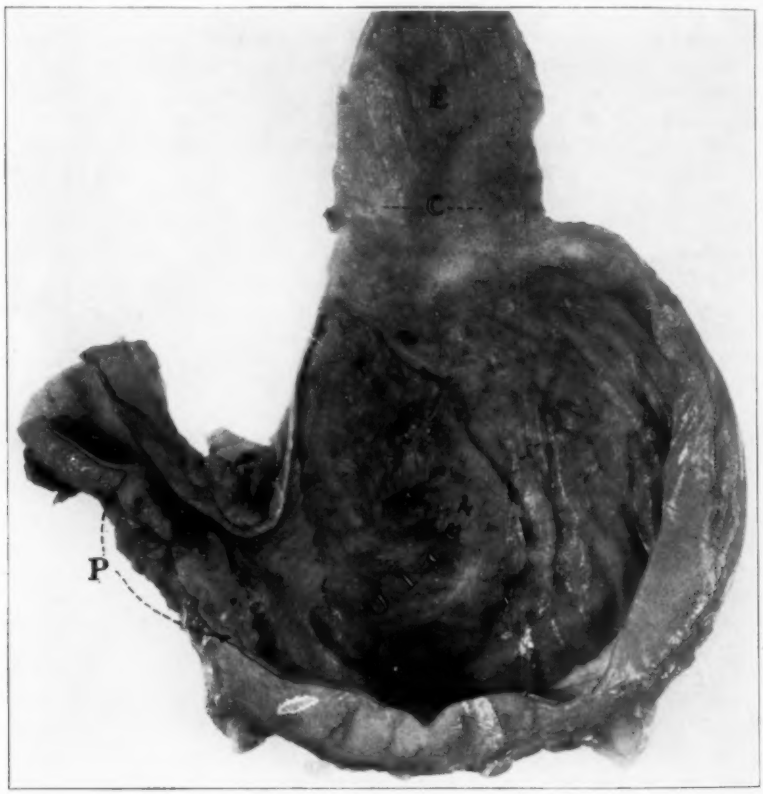

Fig. 2 (case 1).—A syphilitic stomach in which the greater portion of the anterior wall has been removed. The granulomatous infiltrate has encircled the pars pylorica (*P*) and transformed it into a narrow tube. The plaquelike thickening of the gastric wall extends along the lesser curvature almost to the cardia (*C*). An extensive, superficial ulcer of serpiginous outline occupies a considerable portion of the surface of the plateau formed by the granulomatous plaque. The esophagus (*E*) is moderately dilated.

dilated pars cardiaca and pars media. The cylindric portion represented a thickened, contracted pars pylorica, which projected like a spout from the remainder of the stomach. The lesser curvature was contracted, measuring 10 cm. The

greater curvature was 35 cm. long. The serosa over the distal portion of the stomach was thickened, white and edematous; in one area on the lesser curvature side, it was rendered quite opaque. The thickening of the serosa extended to involve the covering of the beginning duodenum distally and especially the lesser curvature and posterior wall proximally. On palpation, the distal 4 cm. of the stomach was firm, elastic and thick. Passing toward the cardia along the lesser curvature, the sense of thickness and resistance imparted by the pyloric portion gradually diminished as the esophageal end was reached. The same palpatory observations were made with regard to a plaquelike area involving the anterior and posterior surfaces for a distance of 5 cm. from the lesser curvature. The margins of this thickened plaque passed almost imperceptibly into the surrounding gastric wall.

When the stomach was opened, the pyloric portion was found to be transformed into a more or less concentric tube with a very narrow opening, roughly of funnel shape. The point of maximum constriction was just at the pyloric ring, where the lumen barely admitted a narrow probe. The lining of the tubular portion was rough and mottled gray-red, was firmly attached to the underlying layers and presented areas of wrinkling and puckering. The intact mucosa merged proximally with an extensive shallow ulcer, which corresponded to the area of plaquelike thickening observed on palpation. The ulcer was quite superficial, the outline somewhat serpiginous, the margins in places barely thickened, and the floor covered by a gray, loosely adherent, lardaceous material. In no place did the base of the ulcer extend below the level of the intact mucosa.

Cross-section of the wall of the stomach showed the thickening of the tubular pyloric portion to be due mainly to an increase of both the submucosa and the muscularis. The maximum thickness of the muscular coat was 5 mm., that of the submucous layer 7 mm. The thickness of each layer diminished very gradually in passing proximally until the cardiac end of the ulcer was reached. The submucosa, on section, was white and homogeneous and appeared fibrous.

Septums of whitish fibrous tissue were found in places extending into the muscularis, which in other respects presented a normal appearance. In the involved areas, the mucosa was decreased and the serosa increased in thickness. The portion of stomach free from infiltrate showed, on cross-section, a slightly thickened muscular coat and a thinned mucosa. The submucosa was grossly normal. The attached portion of esophagus was dilated to measure 6 cm. in circumference. Its musculature was likewise hypertrophied. The perigastric lymph glands were generally enlarged, but none exceeded 1.2 cm. in diameter. The glands were semielastic, gray-pink and moist, and on cross-section presented a relatively normal appearance.

Microscopic Observations.—For the sake of brevity merely the outstanding changes will be included. Detailed descriptions of practically identical lesions can be found in previous reports of other cases that we have studied. The mucosa proximal to the large ulcer was thin and contained atrophic glandular elements, which were relatively widely separated. The tunica propria was infiltrated mainly by lymphocytes. Plasma cells and leukocytes were present in small numbers. In one area, the cylindric was replaced by squamous epithelium composed of from 9 to 14 layers of flat cells, which rested on a dense connective tissue base (leukoplakia). In the ulcerated portion, the mucosa was completely destroyed or substituted by a layer of fibrillar connective tissue, which merged with the submucosa. The muscularis mucosae in the ulcerated area was incomplete, being replaced in

part by fibrous elements. Where still preserved, the muscle fibers presented a hypertrophic appearance and were separated by connective tissue.

The submucosa constituted the base of the ulcer over all but a limited portion of its extent. The floor of the ulcer was covered by a thin layer of fibrinoid necrosis and degenerated leukocytes. The submucous coat began to increase in thickness just proximal to the margin of ulceration. As the center of the defect was approached, the maximum thickness of the submucosa was attained. Here it occupied three fifths or more of the gastric wall. This increase was due to young

Fig. 3 (case 1).—A photomicrograph of an area in the submucosa illustrating particularly the panvasculitis (hematoxylin and eosin preparation). By special stains (elastica and van Gieson) the infiltrating cells are found to be within and surrounding the walls of blood vessels (see fig. 4). An endarteritis has led to sufficient intimal proliferation to obliterate the vascular channels.

granulation tissue rich in fibroblasts, infiltrated by scattered and grouped lymphoid cells. The blood vessels in this layer showed evidence of severe damage. Indeed, it was only by means of special stains (elastica and van Gieson) that the presence of some of the preexistent vessels could be demonstrated. The panvasculitis is so well exhibited in the accompanying photomicrographs (figs. 3 and 4) that a detailed description would prove superfluous. It may be necessary to add that the infil-

trating cells were mainly lymphoid in type. Plasma cells and macrophages were relatively sparse. The veins were involved to a greater extent than the arteries.

The muscularis propria presented slight thickening of its fibrous septums, within which were found small numbers of lymphoid cells. The serosa was increased to several times its normal thickness owing to proliferated fibrous elements and many leukocytes and lymphoid cells. The only other pertinent microscopic changes were noted in the perigastric lymph nodes and the liver. In the former, the follicles of the cortex were small, and their centers were formed chiefly by swollen and proliferated reticulum cells. The medulla contained numerous plasma cells. Sec-

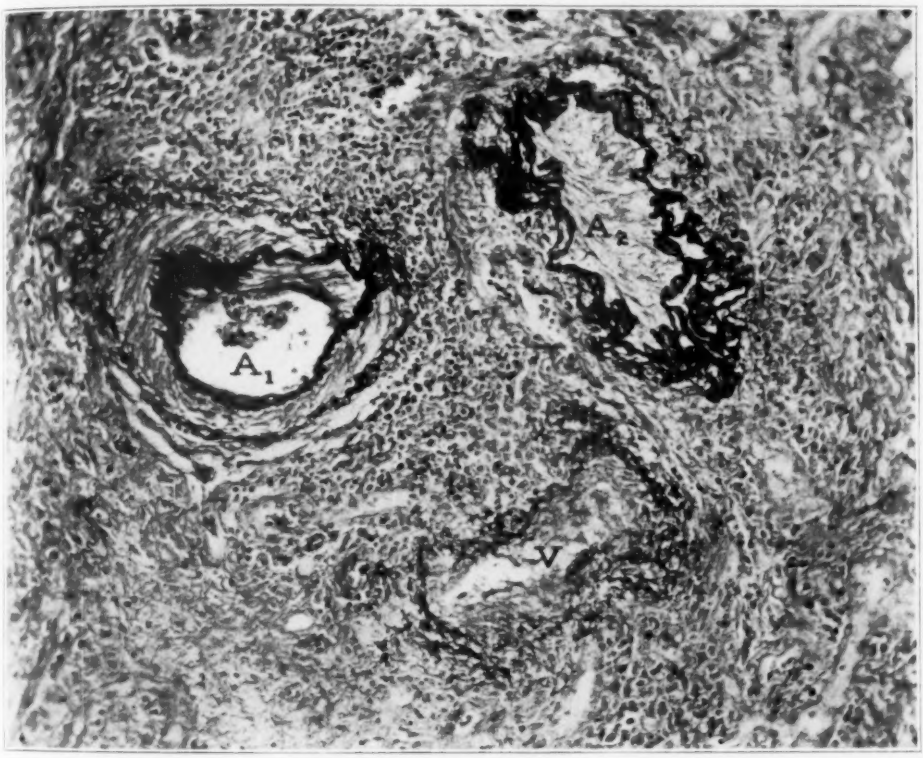

Fig. 4 (case 1).—An elastica preparation from the same block as that shown in figure 3 but somewhat deeper. The elastic fibers of the vein (V) are split and frayed to form a complex network. The internal elastic membranes of the arteries (A_1, A_2) are greatly thickened.

tions from a depressed area in the right hepatic lobe showed a thick strand of dense connective tissue which branched and extended into the hepatic parenchyma. The fibrous strands contained small, thick-walled arteries, bile ducts and scattered and grouped lymphoid cells.

Levaditi preparations contained a moderate number of argentaffine bacilli but no spirochetes bearing a morphologic resemblance to Spirochaeta pallida. Ziehl-Neelsen stains failed to demonstrate any acid-fast organisms. Animal inoculations were not employed.

CASE 2.—J. T., a colored man, aged 28, was admitted to the medical service of the Cook County Hospital on June 11, 1930. On entrance to the hospital his condition was diagnosed as peptic ulcer. He asserted that the very first indication of a gastric disturbance occurred in December of 1929 about six months prior to his hospitalization. He then began to notice epigastric distress occurring from fifteen to thirty minutes after meals and continuing for approximately an hour. The pain was sharp during the first fifteen minutes and gradually subsided following that time. Soda afforded only incomplete relief. Bland foods were better tolerated than coarse or irritating foods.

Fig. 5 (case 2).—An irregular, annular constriction of the prepyloric region produced by gastric syphilis prior to treatment.

Vomiting first made its appearance on April 10, 1930, about four months after the onset of the epigastric pain. Emesis was repeated several times during that day and the following day also. Constant pain was present throughout the period of vomiting. The patient consulted a physician, who prescribed Sippy management for ulcer. The patient felt greatly improved, although he continued to vomit at intervals until after the second week of treatment when he was entirely relieved. After three weeks he returned to an unrestricted diet, following which his pain reappeared. On June 7, 1930, four days prior to entrance, persistent vomiting recurred, on account of which the patient sought admission to the hospital.

A general inventory of symptoms by systems yielded no significant information. The patient admitted a gonorrheal infection a year previous, but stated that he had

no knowledge of a chancre. The results of physical examination were essentially negative, except for moderate tenderness in the epigastric region. The first Ewald meal, recovered after forty-five minutes, yielded 300 cc. of poorly digested material with a free acidity of 30 degrees and a total acidity of 70 degrees. A motor meal aspirated six and one-half hours after ingestion contained recognizable food elements in the form of spinach and raisins. A series of stools were weakly but persistently positive for blood. The Wassermann reaction of the blood was reported

Fig. 6 (case 2).—X-ray film taken two and one-half months after that shown in figure 5, following gastro-enterostomy and a course of antisyphilitic treatment. The degree of narrowing of the prepyloric segment has increased and the deformity has assumed a bizarre outline.

four plus; the Kahn, two plus. The filtered gastric contents gave negative complement fixation, with the use of 0.5 cc. of the fluid. A barium meal revealed (fig. 5) a constant deformity of the pyloric portion of the stomach with obstruction, which were interpreted by the roentgenologist, Dr. C. H. Warfield, as being due to either syphilis or carcinoma.

The patient continued to vomit irregularly on a regimen for patients with ulcer, which included a bland diet. Without attempting antisyphilitic treatment, his

attending physician recommended exploration. The patient was transferred to the surgical service on June 27, 1930, with the diagnosis of gastric syphilis or carcinoma. On the following day, laparotomy was performed by one of us (K. A. M.). The stomach, which was somewhat enlarged, was found to be free from adhesions. Inspection showed the serosa of the prepyloric portion of the stomach to be thickened, whitish and edematous. No tumor mass was visible. Palpation indicated increased thickening of the prepyloric region, but the wall remained fairly pliable. The consistency of the involved area was doughy to semielastic rather than firm as in a scirrhus. The thickening extended to and encroached on

Fig. 7 (case 2).—Histologic appearance of the biopsy specimen removed from the stomach at operation. Except for the upper margin, which consists of gastric tubules and muscularis mucosae, the section is comprised of thickened submucosa. The increase of the submucous layer is due to connective tissue proliferation and cellular infiltration. A perivascular arrangement of the round cells is noted in connection with a venule (*V*).

the pyloric sphincter, causing narrowing of the orifice. No actual tumor mass was palpable. Incision in the longitudinal axis of the stomach into the involved area at its proximal margin showed that the thickening of the wall was due mainly to an increase in the submucous layer, which presented the appearance of edematous, fibrous tissue. Inspection of that portion of the lesion situated distal to the incision showed a superficial ulcer of serpiginous outline, covered with a grayish, lardaceous membrane. Tissue for biopsy was removed from the proximal

margin of the infiltrate and the gastrotomy opening closed. The glands along both curvatures in the prepyloric region were enlarged up to 1 cm. in diameter. They were pink and relatively soft; on cross-section of one of them, no tumor deposits were noted. There were a number of scars in the capsule of the liver involving mainly the left lobe. A posterior gastro-enterostomy was performed. In the meantime, the frozen section of the specimen taken for biopsy was reported as showing chronic inflammation with no evidence of carcinoma.

The patient made an uneventful recovery. During convalescence he was placed on antisyphilitic treatment, which was continued until he left the hospital on Aug. 9, 1930. Roentgen examination (fig. 6) of the stomach on Aug. 30, 1930, showed the prepyloric region to be irregularly deformed and the degree of narrowing to be greater than in the original examination. The barium left the stomach mainly through the gastro-enterostomy opening, which appeared to function adequately.

The material removed for biopsy was used for histologic and bacterioscopic examinations and for biologic tests. The testicular inoculation of a saline suspension of the finely divided tissue into two rabbits failed to lead to the development of a scrotal chancre. Dark field examination of a portion of the suspension did not disclose Spirochaeta pallida. Sections stained according to Levaditi contained no demonstrable spirochete.

Microscopic Observations.—Material submitted to Dr. A. S. Warthin was reported by him as follows: "No positive signs of syphilis histologically. Lymph node shows nothing suspicious of syphilis and there is nothing in the scar that would indicate lues. Moreover, spirochete examination is entirely negative." Sections from other areas sent to Dr. Warthin drew the following comment: "Additional material: Chronic inflammation. Fibrosis. Callus of healed ulcer. No evidence of syphilis." Our own description of the histologic preparations of the remaining tissue follows: The wall of the stomach was moderately thickened owing to an increase mainly of the submucous layer. The mucosa showed increased cellularity of the tunica propria. The infiltrating cells were chiefly of the lymphoid type, although eosinophilic leukocytes were relatively abundant. The muscularis mucosae was interrupted and divided by proliferated connective tissue and contained many foci of round cells. The submucosa was several times the normal thickness owing to an increase in the fibrous elements together with infiltrations by scattered and grouped lymphoid and plasma cells. The blood vessels in this layer were increased in thickness, but showed no tendency to obliteration. Occasionally, the infiltrating cells assumed a perivascular arrangement (fig. 7). In general, the walls of the vessels were free from invasion by wandering cells. The muscularis propria supported accumulations of round cells, but was otherwise unchanged. The serous coat was edematous and slightly thickened by virtue of the presence of proliferated connective tissue and infiltration by lymphoid cells.

COMMENT AND SUMMARY

The responsibility of recognizing the presence of syphilis of the stomach at the operating table logically falls on the surgeon. A frozen section made of tissue removed for biopsy during operation is of relatively little aid in establishing a diagnosis of gastric syphilis. The value of the microscopic preparation, provided the block of tissue is properly chosen, lies chiefly in the exclusion of carcinoma. The diagnosis can best be made by a consideration of the gross characteristics of the lesion.

It is on this account that a knowledge of the macroscopic attributes of the condition is of considerable importance to the gastric surgeon.

The features that serve to distinguish syphilis of the stomach from carcinoma, which is most closely simulated, are as follows: There is a striking disparity in many cases between the extent of the lesion as determined roentgenologically and the extent as observed operatively by palpation. Whereas in carcinoma one generally finds at laparotomy a more extensive involvement than the x-ray picture indicates, in syphilis of the stomach there is a surprising paucity or complete absence of changes as determined by palpation. The common lesion of gastric syphilis is not a spherical prominence as in a tumor, gummatous or neoplastic, but is a flat infiltrate that leads to a plaquelike thickening of the gastric wall. When thin, the infiltrate is readily overlooked. When thick, its relatively soft consistency and pliability distinguish it from carcinoma. On cross-section, the increase is seen to be due to an edematous fibrous tissue located chiefly in the submucosa. Inspection of the interior of the stomach generally discloses one or more superficial, serpiginous ulcers involving a large part of the plateau formed by the infiltrate. The base of the syphilitic ulcer, contrary to the peptic variety, is situated at a higher level than the normal mucous membrane. Fibrous and edematous thickening of the serosa and adhesions, when present, suggest an inflammatory rather than a neoplastic lesion. Associated syphilitic changes that may be detected during the course of the operation include hepatic, intestinal and splenic syphilis. Of these, the co-existence in the liver of gummas, deep stellate scars or subtotal destruction of the left lobe is of greatest aid in the recognition of the type of gastric disease present.

In the two cases described here, the gross features of the gastric lesion led to the correct diagnosis in each instance. The first patient was operated on by a surgical colleague who, on palpating the stomach, immediately apprehended that he was dealing with an unusual condition. A verbal description of the physical characteristics led us to predict with confidence that the involvement was syphilitic. The diagnosis in the second case was based chiefly on the observations made at operation, since from biopsy the condition was reported as simple nonspecific inflammation. The associated data, particularly the beneficial effect of antisyphilitic treatment and the subsequent course, lend strong support to the macroscopic diagnosis.

RESECTED KNEE JOINTS

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In spite of advance in knowledge and the great increase in surgical operations with their consequent revelations, there are many diseases of the knee joint that cannot be diagnosed definitely. The study of pathologic specimens which include the entire joint is of significance, but such specimens are relatively rare. The knee joint is seldom examined at necropsy, and various surgical procedures, although affording macroscopic examination, give little material for pathologic research. The operation of resection, however, makes it possible to secure a large enough specimen so that a conception may be formed of the pathologic changes in the joint. The important structures of the joint are all included in such specimens and they can be studied collectively to visualize a definite picture of the changes present. Resection has been performed extensively at the Mayo Clinic for many years, during which valuable data have accumulated.

MATERIAL STUDIED

Records of 236 resections or fusion operations and 9 amputations performed for disease of the knee joint in the years from 1919 to 1931, inclusive, were reviewed. Many of the pathologic specimens were fragmented or incomplete, but 120 were intact, and these were selected. In order to form a basis for comparison in the cases of tuberculosis of the knee joint, the histories of all such cases seen during this same period were reviewed. In 117 cases some type of minor surgical operation was carried out, such as aspiration or cast, and in 139 no treatment was given, patients having been seen in consultation and advised to have treatment elsewhere. A total of 501 case histories was examined.

In 245 cases in which operation was performed, the incidence of trauma or infection as inciting or predisposing factors, the duration of symptoms and the age and sex of the patients were noted. In 168 of these cases (68.6 per cent) tuberculosis was found by microscopic study or by inoculation of guinea-pigs. In 66 cases (27.7 per cent) non-

From the Section on Orthopedic Surgery, the Mayo Clinic.

tuberculous inflammatory lesions were the cause of the destructive process. These cases included the end-results of septic joints, old traumatic joints, extensive proliferative arthritis and old osteomyelitis with involvement of the joints. Nine cases were listed as atrophy; 8 of these were anterior poliomyelitis in which fusion or resection of the knee was performed, and there was a case of painful atrophy due to disuse in which resection had been done. Besides these cases, there were 2 of Charcot's joint.

Of the tuberculous patients, males outnumbered females 2.5:1. The ratio in nontuberculous patients, however, was 1.2:1. The 2 patients with Charcot's joints were males. The group of patients with atrophy from disuse included 4 males and 5 females. Most of the patients operated on were between the ages of 20 and 40 years; 68.6 per cent were in the tuberculous group, and 57.7 per cent in the nontuberculous group.

ONSET

In 1807, Cooper [1] pointed out the tuberculous predisposition to be noted in many cases and the effect of injury in producing local lesions. Trauma has since been emphasized by many writers as a predisposing factor in disease of the knee joint. Schüller [2] and Krause,[3] who injected the bacillus of tuberculosis into animals, reported that injury to bone and joint tissue was a definite localizing factor. Friedrich,[4] on the other hand, found that traumatized joints were less likely to become involved, and Fraser [5] regarded trauma as of more significance in disseminating disease if a quiescent focus existed, than in localizing the disease primarily. It was his belief that slight trauma localizes a tuberculous process, but that severe trauma causes a reactive state in the tissue which destroys the bacillus of tuberculosis. Salvia [6] stated that trauma in flat bones always determines the site of the lesion, whereas in long bones no definite influence is exerted.

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1. Cooper, Samuel: A Treatise on the Diseases of the Joints, London, R. Phillips, 1807.

2. Schüller, M.: Experimentelle und histologische Untersuchungen über die Entstehung und Ursachen der skrofulösen und tuberkulösen Gelenkleiden, Stuttgart, Ferdinand Enke, 1880.

3. Krause, Fedor: Die Tuberkulose der Knochen und Gelenke, Leipzig, F. C. W. Vogel, 1891.

4. Friedrich, P. L.: Experimentelle Beiträge zur Kenntnis der chirurgischen Tuberkulose, Deutsche Ztschr. f. Chir. **53**:512 (Nov.) 1899.

5. (*a*) Fraser, John: An Experimental Study of Bone and Joint Tuberculosis, J. Exper. Med. **17**:362 (March) 1913. (*b*) Tuberculosis of the Bones and Joints in Children, London, A. & C. Black, Ltd., 1914.

6. Salvia, Edoardo: L'influenza dei piccoli traumi sulla localizzazione della tuberculosi, Policlinico (sez. chir.) **11**:367, 1904.

In our series of cases, only 39.8 per cent of the patients with tuberculosis and 39.4 per cent of those without tuberculosis gave a history of previous injury which might in any way have been an inciting cause. Such injuries varied from a slight bruise to a fall from a telephone pole. Practically the same percentage of traumatic background was presented by male and female patients, which suggests that the severity of the injury matters little so far as a predisposing factor is concerned. Some writers are definitely of the opinion that slight sprains or bruises are more likely to be localizing factors than fractures or dislocations.

TABLE 1.—*Onset of Disease*

	Tuberculous		Nontuberculous Arthritis	
	Cases	Per Cent	Cases	Per Cent
Trauma				
Total	67	39.8	26	39.4
Male	48	40.6	16	44.4
Female	19	38.0	10	33.3
Following infection	8	4.7	12	18.2
Idiopathic	93	55.4	28	42.4

TABLE 2.—*Infectious Type*

	Tuberculous	Nontuberculous
Following		
Typhoid fever	1	1
Scarlet fever	1	..
Osteomyelitis	..	3
Pneumonia	2	..
Gonorrhea	..	2
Rheumatic fever	..	2
Influenza	1	1
Influenza, scarlet fever and tonsillectomy	1	..
Scarlet fever and typhoid fever	..	1
Measles and bronchitis	1	..
Encephalitis	..	1
Tonsillitis	..	1
Lymphangitis of leg	1	..

Four and seven-tenths per cent of the patients with tuberculosis and 18.2 per cent of those without tuberculosis were observed from a few days to several months after some form of acute infection had been manifested elsewhere in the body (tables 1 and 2). It may be noted that in 5 of the 8 cases of tuberculous arthritis with preceding acute infection, the condition followed a respiratory disease, whereas in only 1 of the 12 cases in which tuberculosis was not present was this true.

DURATION OF THE DISEASE

In 55.8 per cent of all cases the disease had existed prior to operation more than five years. The shortest duration of symptoms in the tuberculous cases was three months, the longest, thirty-nine years, and in the nontuberculous cases, four months and thirty-three years,

respectively. Patients with Charcot's joints gave a history of duration of five and two years.

In the 256 cases in which tuberculosis was present and operation was not performed, variation from these figures was noted only in age incidence and duration. The proportions of males and females were the same, and the percentage of cases in which inciting trauma was apparent was even lower, 36.6 per cent. In this group only 35.8 per cent of the patients were between the ages of 20 and 40 years; the majority, 50.3 per cent, were in the first two decades of life. The youngest patient was aged 14 months and the oldest 73 years. In only 25.6 per cent of this group of cases was the duration of the disease more than five years; the shortest duration was two weeks, and the longest was more than thirty years. These facts seem to show that age was an important factor in the selection of cases for operation. Only 0.6 per cent of the patients in the operative group were aged less than 11 years, as compared with 30.9 per cent of those not operated on. Furthermore, the higher incidence of short duration of symptoms among patients not operated on reveals the tendency to avoid radical procedures as long as possible with the hope of relief by some other means. This is most striking when the duration was one year or less; there were 30.2 per cent of these patients among those not operated on, as compared with 5.3 per cent among those who were operated on.

GROSS SPECIMENS

From 245 cases in which operation was performed, 120 whole specimens were obtained. These included the articular surfaces of the tibia, most of the articular surfaces of the femur, varying amounts of synovial membrane, and in more than half of the cases, the entire patella. One hundred and two of the specimens were tuberculous, 17 were nontuberculous and 1 specimen was a Charcot joint. Since the clinical symptoms had existed from three months to thirty-nine years, the pathologic changes in the specimens were varied. In some cases there was marked destruction of all the structures of the joints. In others the tissues were practically intact. In comparing the specimens and histories, we found the progress of the nontuberculous types of infection more rapid than the tuberculous type as a general rule. This same observation was made by Koenig [7] in 1884. His work on the subject of tuberculosis of bones and joints has received widespread corroboration and but little significant contradiction.

As a rule, in cases of tuberculosis of short duration of symptoms, there is only slight pathologic change; usually early pannus formation

7. Koenig, Franz: Die Tuberculose der Knochen und Gelenke, Berlin, A. Hirschwald, 1884.

is present, or slight invasion of margins of bone. The cartilage is intact in most cases. In the cases in which tuberculosis is not present there is, as a rule, advanced change in the structures of the joint, particularly the cartilaginous structures, with some destruction of bone (figs. 1 and 2). In advanced cases marked destruction may accompany both types of infection, and they are often indistinguishable grossly. Exceptions, however, are not uncommon. In several cases of tuberculosis of long duration there was little destruction. In one case, in which the clinical history covered more than fifteen years, only the

Fig. 1—Tuberculous joint of three years' duration.

external surfaces were affected (fig. 3). This illustrates the ability of tuberculosis to become walled off almost completely in one compartment of a joint, destroying that part and leaving the remainder fairly free. Certain specimens, however, disclosed much more rapid progress of the disease in the cases in which tuberculosis was present and slow progress in those in which it was not present. In a case in which tuberculosis was not present, only the external surfaces were involved after twenty-two years of symptoms.

The question of whether the site of origin of tuberculosis of the joint is in the synovia or bone has been discussed for many years.

Berry [8] stated that most older writers, including Billroth, favored a synovial origin, whereas Volkmann, Schüller, Virchow and several others felt that the primary lesion was in the bone. More recently, Fraser [5b] has advanced the opinion that tuberculosis of the joint is definitely synovial in origin. Rogers,[9] Stiles [10] and Smith [11] believe this to be true in the majority of cases. Nichols,[12] on the other hand, thought that a focus in bone existed in every one of his specimens. Koenig [7] stated

Fig. 2—Nontuberculous specimen of one year's duration (compare with fig. 1).

8. Berry, J. J.: Articular Osteitis of the Knee in Children, M. Rec. **17**:113, 1880.

9. Rogers, M. H.: Tuberculosis of the Knee-Joint in Adults, Am. J. Orthop. Surg. **12**:589 (April) 1915.

10. Stiles, H. J.: The After-Results of Major Operations for Tuberculous Disease of the Joints, Brit. M. J. **2**:1356 (Nov. 16) 1912.

11. Smith, A. DeF.: The Pathology of Joint Tuberculosis in Its Earlier Stage, Arch. Surg. **12**:740 (March) 1926.

12. Nichols, E. H.: Tuberculosis of Bones and Joints, Tr. Am. Orthop. A. **11**:353, 1898.

that the origin might be either in bone or synovia; Ely [13] and Phemister [14] also adopted this view. In 56 per cent of our gross tuberculous specimens the process was advanced, both in bone and synovial membrane, so that it was impossible to ascertain the primary site. Of the remaining specimens, 37.2 per cent appeared to be primarily in the synovial membrane, whereas only 6.8 per cent disclosed evidence of a primary lesion in the bone. The distinction is difficult and, as will be shown, is of little

Fig. 3—Tuberculous knee of fifteen years' duration. There is destruction of the external surfaces and the patella. The cartilage of the internal surfaces is well preserved.

practical significance. In all of our specimens both synovial membrane and bone were involved, so that from the surgical standpoint tuberculosis was not limited to either bone or synovial membrane; undoubtedly

13. Ely, L. W.: Joint Tuberculosis, with Special Reference to Its Pathology, M. Rec. **76**:551 (Oct. 2) 1909.

14. Phemister, D. B.: Changes in the Articular Surfaces in Tuberculous Arthritis, J. Bone & Joint Surg. **23**:835 (Oct.) 1925.

this may occur, but almost invariably it is before a diagnosis can be made. When tuberculosis becomes sufficiently advanced to make possible a clinical diagnosis, it has spread to both structures. Pasquali,[15] in a recent report of 156 resections of the knee at the Instituto Rizzoli, mentioned 3.8 per cent as purely synovial in origin, 3.2 per cent as in the bone and 93 per cent as osteo-arthritic.

In 94.1 per cent of the cases in which tuberculosis was not present, the lesion appeared to be of synovial origin. In only a single case was there question of a focus of infection in bone. In all cases opinion was based on the condition of the articular surfaces, the appearance of the cut surfaces and the condition of the bone as seen by sections through the surfaces of the joint.

Various writers have observed certain sites of predilection for the origin of tuberculosis. Ely [16] stated that the head of the tibia is the most common starting point. Fraser [17] thought the lower end of the femur was the most common primary site of the disease. Kolodny [18] believed the external epicondyle to be the favorite site because of its more extensive circulation. Henderson [19] noted that it is not extremely rare to find the disease originally in the patella. In 52.6 per cent of our tuberculous specimens, the site of the primary lesion could not be determined. In 34.4 per cent the site was apparently in the tibia, in 10 per cent it was in the femur and in 3 per cent in the patella. In the nontuberculous specimens the point of origin seemed to be equally distributed between the tibia and the femur; the patella was primarily involved in a case. Because of the rapid progress of the disease, it was difficult to ascertain the primary site.

It is the general belief that in the presence of inflammatory lesions of the joints, cartilage is never primarily affected but is passively invaded and destroyed by surrounding disease. In studying the tuberculous specimens, we found that the cartilage seemed to be attacked from three sources: (1) the overlying pannus formation springing from the synovial membrane at the margins; (2) the subchondral granulation tissue spreading along beneath the cartilage and usually arising from

15. Pasquali, E.: Esiti della resezioni viella tuberculosi del ginocchio, Bibliog. Orthop. **11**:193 (June) 1931.

16. Ely, L. W.: Joint Tuberculosis, New York, William Wood & Company, 1911.

17. Fraser, John: Observations on the Situation of the Lesions in Osseous Tubercle, Edinburgh M. J. **9**:436 (Nov.) 1912.

18. Kolodny, Anatole: A Contribution to the Knowledge of Pathogenesis of Skeletal Tuberculosis, J. Bone & Joint Surg. **23**:53 (Jan.) 1925.

19. Henderson, M. S.: Tuberculosis of the Knee Joint in Children, Minnesota Med. **3**:463 (Oct.) 1920.

the margins of the surface of the joint, at times lifting the cartilage free of the bone and at times perforating the cartilage, and (3) the destruction taking place through erosion of the surfaces of the joint chiefly at the areas of pressure. In the nontuberculous specimens pannus formation was slight, the cartilage apparently being destroyed chiefly by the effect of pressure or by digestion due to toxic products of infection within the joint, or by both of these factors. In the tuberculous specimens the persistence of portions of the cartilage over many years was often observed. In the nontuberculous specimens, however, whenever cartilage had been destroyed, it had been removed and replaced by fibrous tissue, or ankylosis was present in various stages of activity.

Phemister [20] demonstrated the basis for these different reactions. In our tuberculous specimens there was good preservation of cartilage in 16.6 per cent of the cases, destruction of varying severity in 80.4 per cent and only partial involvement of the surfaces in 3 per cent. In the nontuberculous specimens there was fairly good preservation in 11.7 per cent, destruction (usually more severe than in the tuberculous specimens) in 70.6 per cent and only partial involvement in 17.7 per cent. In the nontuberculous specimens destruction was always greater at the areas of pressure of the surfaces of the joint. This corroborates the observations of Phemister, who found that the cartilage attacked by proteolytic ferments of the exudate of the joint is vulnerable to the pressure from the opposite surface of the joint and the most extensive erosion takes place at this point. In tuberculosis, however, he found a marked scarcity of these proteolytic ferments, which might account for the slow progress of the disease and the preservation of cartilage at the areas of pressure.

In our tuberculous specimens, there was no definite rule as to the point of greatest destruction of cartilage. Koenig [21] first expressed the opinion that in tuberculosis the cartilage is destroyed chiefly at areas where pressure is absent. According to Phemister,[14] "articular cartilage may be affected: (1) by the direct action of tubercle toxins, (2) by tuberculous granulation tissues and (3) by the pressure erosion in opposing articular surfaces." He explains the growth of the pannus over the surface of the joint, the areas of pressure being kept clear of pannus by friction, but as the joint becomes more involved and less motion takes place more of the auricular surface becomes covered. Phemister has shown how, in severe cases, there may be two types of

20. Phemister, D. B.: The Effect of Pressure on Articular Surfaces in Pyogenic and Tuberculous Arthritides and Its Bearing on Treatment, Ann. Surg. **80**:481 (Oct.) 1924.

21. Koenig, Franz: Die Tuberculose der Knochen und Gelenke, Berlin, A. Hirschwald, 1896.

change which greatly alter the picture from that which is seen in the less severe forms, i. e.:

First, there may be caseation of the tuberculous granulations, and those overgrowing the surfaces of the articular cartilage are equally affected with those involving the synovial membrane. This early caseation may either entirely prevent the overgrowth of granulations on the cartilage or rapidly remove those that have formed, so that destruction by direct attack of tuberculous tissue along the free surface of the cartilage is either limited in amount or entirely lacking. A second effect of severe tuberculous arthritis may be the production of necrosis of large areas of articular cartilage, partly by the action of the tubercle toxins and partly by cutting off of nutrition from the normal synovial fluid. . . . When the infection is sufficiently severe to kill articular cartilage, it may do so in the regions of contact and pressure of opposed articular surfaces, as is the case in severe pyogenic arthritis.

Fig. 4.—Tuberculous knee of ten years' duration. Marginal pannus formation and cartilaginous destruction with preservation at the areas of pressure are shown.

Our specimens have demonstrated that the preservation of cartilage at the areas of pressure cannot be depended on as a diagnostic factor in favor of tuberculosis of the knee (figs. 4 and 5). In 29.4 per cent of the cases there was greater destruction of cartilage at the margins of the joint. In 20.6 per cent the destruction was definitely greater at the areas of pressure. In 44.1 per cent distinction could not be made because of advanced destruction, while in 5.9 per cent the different surfaces of the

joint presented dissimilar changes, some showing greater destruction at the center and others at the periphery.

The comparatively large number of cases in which there was central destruction suggested that prolonged weight-bearing might be a cause of the variation. Examination of the histories disclosed that about half of the patients had been receiving treatment designed to relieve the effect of weight-bearing. Approximately the same proportion of

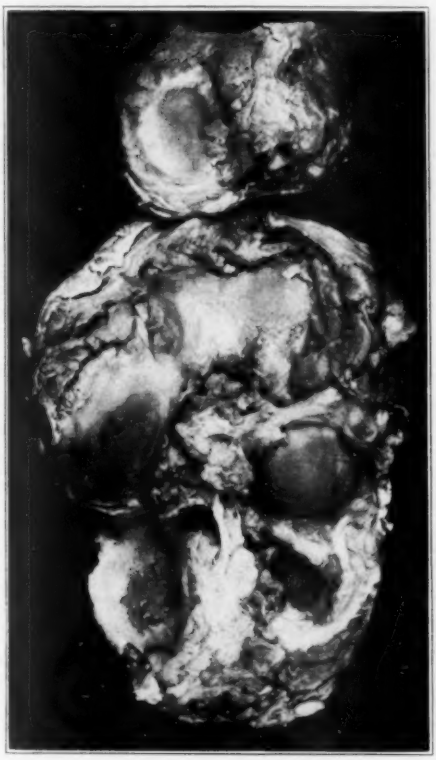

Fig. 5.—Tuberculous knee of one year's duration. Destruction of cartilage at the areas of pressure and contact with preservation at the margins are shown. A tuberculous pannus has extended across the external condyle just above the pressure.

exposure to pressure existed in the presence of destruction of margins, so that this factor was probably not responsible for the divergent cartilaginous changes.

In 85.2 per cent of the cases in which there was greater marginal destruction, the pannus was nodular and luxuriant; it was caseous in 7.4 per cent and fibrous in 7.4 per cent. The original lesion was apparently synovial in 70.3 per cent and questionable in 29.7 per cent. In 45 per

cent of the cases of greater central destruction, the pannus was nodular and luxuriant; it was caseous in 25 per cent, fibrous in 5 per cent and entirely absent in 25 per cent. The original lesion was apparently synovial in 55 per cent, bony in 5 per cent and questionable in 40 per cent.

There are several possible reasons for the increased destruction at areas of pressure. As Phemister has claimed, there is a higher percentage of cases of central destruction with caseous pannus than of marginal destruction; this means less peripheral destruction and greater toxicity of joint fluid with less resistance of the central cartilage to pressure. The number of cases in which there is no pannus formation is significant. Ordinarily the marginal pannus forms a peripheral cushion which receives part of the weight from the opposing surface of the joint, and tends to relieve the strain on the area of pressure. When it is absent, the central area is in no way protected from the effects of pressure and subchondral disease. Finally, a greater percentage of questionable foci in bone in cases of central destruction may be of some significance. The effect of the subchondral changes will be considered under microscopic sections. In our nontuberculous specimens there was pannus formation in only 2 cases (12 per cent). These were firmly attached to the surface of the joint. In the tuberculous specimens it was seen in 35 cases (34.3 per cent). The pannus was attached only to the synovial reflection in half of these cases; in the remainder it was closely adherent to the cartilage. In 16.6 per cent of the tuberculous specimens abscess of bone was present; it was present in the tibia in 12.7 per cent, in the femur in 1 per cent and in both bones in 2.9 per cent.

The presence of sequestrums in tuberculous joints has been recognized by many writers and noted with varying frequency. In 29 cases (28.4 per cent) we observed these either as bits of bone more or less detached, or more frequently as areas of eburnated bone along the surface of the joint; they were seen in the tibia in 5.9 per cent, in the femur in 6.8 per cent and in both bones in 15.7 per cent. Usually these areas of sequestration were easily seen. In several instances, however, they were completely covered with cartilage and were only discovered by inspection of the cut surface of the bone or by making a section through the joint. Ordinarily such cartilage was badly destroyed but in 1 specimen, an early case, it was apparently intact. Sequestrums appeared in areas of pressure in all except 2 cases, and in these it is possible that the area of pressure had been shifted somewhat, owing to the relaxation of the capsule of the joint. In 13 cases (12.7 per cent) we observed the presence of "kissing sequestrums," or opposing areas of sequestration, in the tibia and femur. Of these, 2.9 per cent

were on the internal surfaces, 8.8 per cent on the external surfaces and 1 per cent was on both the internal and external surfaces. All of these occurred on areas of pressure. In the nontuberculous specimens only 1 sequestrum was found. This was in the external tuberosity.

All of the surfaces of the Charcot joint contained hypertrophied bone. The articular cartilage was entirely absent except in spots at the periphery where some fibrocartilage still remained. The ends of the bones were extensively eburnated, but sequestrums were not observed. Several questionable loose bodies were seen in the fibrous attachment to the tibial tuberosity. No vestige of the capsule of the joint or ligamentous structure remained. The picture was one of advanced destruction of soft tissue with overgrowth of bone.

ROENTGENOGRAMS

A review of the roentgenograms available in these cases showed that again there are many exceptions to the usually accepted rules. One is led to believe that in tuberculous joints there is a characteristic picture of haziness or cloudiness, with later erosion of margins and preservation of the joint space. In the final stages advanced destruction of bone may be evident. Atrophy of bone is usually considered an essential accompaniment of tuberculosis of the joint. In the nontuberculous joint early obliteration of the joint space often with ankylosis of bone is the more commonly accepted picture.

We found it difficult in the early cases to pick out any constant diagnostic features in the roentgenogram which could be said to identify either type of lesion. In the advanced cases again marked difference did not exist, but in the moderately advanced cases changes were found to be more typical. In all cases in which changes are apparent in the roentgenograms the disease is probably well advanced. In cases of tuberculosis the disease is usually well advanced, as far as any hope of checking its spread throughout the joint is concerned, before the patient consults a physician. In cases of nontuberculous infections a more marked change may be seen in a relatively shorter time, but this time period is often too prolonged to make the roentgenogram of very great value as an aid to early diagnosis. In 77 per cent of the tuberculous specimens the roentgenograms disclosed atrophy; hypertrophic changes were apparent in 12.3 per cent, and there was no change in density of bone in 10.7 per cent. In 63.7 per cent of the nontuberculous cases the roentgenograms disclosed atrophy; hypertrophic changes were present in 18.2 per cent. No change was observed in 18 per cent of the cases.

As an index to diagnosis the intact joint space must be regarded with some reservation. Often there is flexion contracture in the knees,

and the joint space cannot be truly represented in the roentgenogram. In most of our cases there was greater destruction of cartilage in the nontuberculous joints for a given duration of symptoms. Compared with the gross specimens there was only a small percentage (9.3 per cent) in the tuberculous cases in which roentgenograms failed to demonstrate cartilaginous changes. In 45.4 per cent of the nontuberculous joints, however, the roentgenograms demonstrated less change than was actually present. From the standpoint of destruction of bone, roentgenograms of both tuberculous and nontuberculous specimens disclosed more than was seen on superficial inspection of the gross specimen. This is due to the subchondral erosion of bone which takes place at the margins of the joint in many cases before the cartilage has been removed. Many areas of destroyed bone are covered by dense pannus or filled with tuberculous granulation tissue so that they are not seen on inspection of the gross specimen unless it is sectioned. Erosion of margins may be seen in nontuberculous specimens so it is not a diagnostic sign in tuberculosis. There was greater destruction apparent in roentgenograms of areas of pressure than at the margins in a large percentage of the tuberculous as well as of the nontuberculous joints. The roentgenograms failed to reveal sequestrums when they were present in a considerable number of cases. Of 20 tuberculous joints with sequestrums in the gross specimens only 7 (35 per cent) were visible in the roentgenograms. Thus too much stress cannot be placed on the interpretation of the roentgenologic findings alone. The roentgenogram is, of course, an essential adjunct to diagnosis, but taken alone it may in many cases be inconclusive and even misleading.

MICROSCOPIC SECTIONS

Sections were cut through the surfaces of joints of the complete specimens in 91 tuberculous joints, in 15 nontuberculous joints and in 1 Charcot's joint. Three types of changes were investigated in all cases, namely, bony, synovial and cartilaginous. Actual section of the tissues of the joint results in the smallest amount of error. The microscopic appearance of tuberculosis has been definitely demonstrated. When inflammatory tissue is present, without collections of epithelioid cells and lymphocytes, then tuberculosis cannot be diagnosed. Giant cells are not necessary for the diagnosis. In fact, foreign body giant cells are often present, acting as osteoclasts or chondroclasts in tissues that are definitely not tuberculous. Unfortunately, since tuberculosis usually spreads slowly, specimens removed from the joint for examination may not contain the lesion, whereas in another portion of the joint the disease may be rampant. In several cases, specimens diagnosed as nontuberculous at the time of operation were found on further investigation of

other areas of the joint to be tuberculous. On the other hand, in many cases in which the pathologist had diagnosed tuberculosis, additional sections were necessary in order to establish the pathologic change. In all diagnostic explorations, therefore, it is necessary to take a goodly amount of tissue for examination, and preferably from many portions of the joint.

Our sections of tuberculous tissue demonstrated the typical lesions, whether nodular, caseous or fibrous. There was evidence in all of the

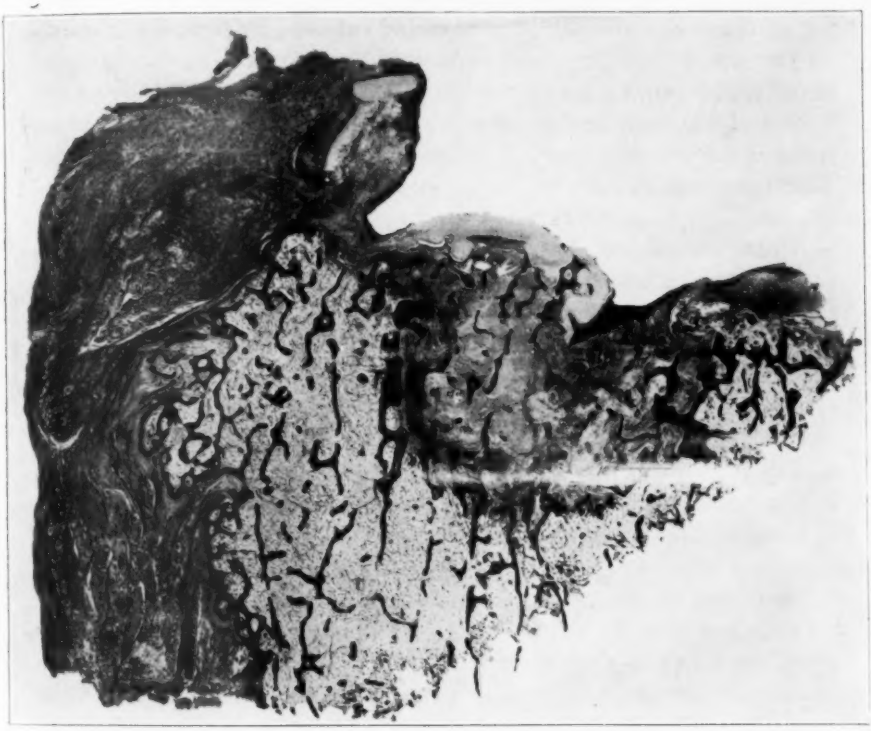

Fig. 6.—Tuberculous subchondral granulations springing from the margins of the joint and dipping down to surround a sequestrum, over which the dead cartilage still remains.

sections of involvement of both synovia and marrow. Therefore, we feel that the distinction between tuberculosis of synovia and bone is futile from a practical point of view. In cases in which the origin was evidently synovial and in which grossly the surface of the joint was almost intact there was marginal infiltration of the marrow and definite invasion of granulation tissue beneath the cartilage. In cases in which the origin appeared to be primarily in the bone, some spread of the infection to the synovial reflection at the margin of the joint was almost invariably present.

Cartilage in all sections appeared to be invaded secondarily. In some cases this was due to a focus in the bone beneath the cartilage eroding and possibly perforating from beneath. Usually, however, it occurred secondarily to marginal involvement of the synovia, either in the form of a tuberculous pannus creeping over the surface of the joint, or as subchondral granulation tissue spreading between bone and cartilage and destroying slowly as it progressed.

The nontuberculous sections manifested little evidence of pannus formation. When present, it was fibrous and adherent. In most cases the cartilage was entirely destroyed and replaced by fibrous tissue. In 40 per cent of the cases subchondral granulation tissue, consisting of fibroblasts, round cells and young capillaries were present between the bone and the cartilaginous remnants. These nontuberculous sections suggested a primary synovial lesion in all cases. In 66.6 per cent of cases there was atrophy of bone. In 20 per cent there was no change, and in 13.4 per cent there was hypertrophy of bone.

In the tuberculous sections the cartilage was fairly well preserved in 13.2 per cent of cases; the remainder showed all grades of degeneration and replacement by fibrous tissue. The bone itself was atrophic in 60.4 per cent of cases and hypertrophic in 3.3 per cent. In 4.4 per cent there was definite abscess formation, in 26.3 per cent sequestrums were present and in 5.6 per cent change was not demonstrable. Of the 24 cases in which microscopic sequestrums were found, they were visible in only 16 of the gross specimens. In 16.6 per cent of the cases pannus formation was not observed. Of those present, 60 per cent were nodular, 11.27 per cent were fibrous and 11.7 per cent were caseous.

Most writers have claimed that subchondral granulations in tuberculous tissue, except at the very margins, show no evidence of tuberculosis. Phemister stated that the tissue is a reaction of foreign body granulation to the degenerated cartilage lying above in an effort to remove it completely. In 58.2 per cent of our sections subchondral granulation was not present. In 29.7 per cent of the cases the subchondral granulations were nonspecific, consisting of fibroblasts, round cells and young capillaries with occasional foreign body giant cells. In 12.1 per cent the tissue was clearly tuberculous in the center of the joint. In several of the cases in which the granulations were classified as nontuberculous, the tissue was of questionable nature, having many of the characteristics of tuberculous tissue without definite cellular arrangement.

Sequestrums were, in some cases, due to foci in bone beneath the cartilage. In others they were apparently due to subchondral granulations dipping down to surround an area of bone, most commonly at an area of pressure (fig. 6). In only one or two instances were sequestrums found at areas where pressure was absent.

In all cases there was either no cartilage over a sequestrum, or the cartilage was fibrillated and dead. This dead cartilage invariably was eroded from opposing pressure, except those occurring at the margins. In all except one case there were no subchondral granulations in an area of sequestration.

In the cases in which there was greater destruction of cartilage at areas of pressure, there was either a sequestrum causing loss of nutrition of the cartilage or a luxurious growth of subchondral granulation tissue; in 40 per cent of the cases this was tuberculous. There seemed to be no hard and fast rules for the microscopic appearance of the lesions, just as we had observed in the gross specimens and in roentgenograms. The changes due to tuberculosis differed considerably in the various specimens. By and large, however, the microscopic examination was by far the most satisfactory.

Sections of the Charcot joint contained a small amount of fibrocartilage covering hypertrophic dense bone. There was considerable formation of new bone and a good deal of osteoid tissue. Fibrosis was present in the marrow spaces near the joint. The cellular elements consisted of a few scattered fibroblasts and round cells. Subchondral granulation tissue was not present.

DIAGNOSIS

The clinical diagnosis of the two principal types of arthritis of the knee under consideration is sufficiently difficult to involve a large percentage of error. In a recent article Milgram [22] has shown that in a fairly large group of proved cases of tuberculosis of the bones and joints, 38.7 per cent were incorrectly diagnosed clinically. Of the unrecognized conditions, 67.3 per cent were not diagnosed by the operators as tuberculous from the gross appearance. One of us (Ghormley [23]) published a similar report in a review of 135 cases of disease of the joints. In 41 cases a diagnosis of tuberculosis was made clinically. In only 66 per cent was this ultimately found to be correct. In 42 cases a diagnosis was made of nontuberculous arthritis. The final diagnosis by examination of tissue in this group was tuberculosis in 38 per cent. Hibbs and von Lackum,[24] Ely [25] and Friedrich [26] reported similar figures.

22. Milgram, J. E.: Diagnostic Inaccuracy in Tuberculosis of Bone, Joint and Bursa, J. A. M. A. **97**:232 (July 25) 1931.

23. Ghormley, R. K.: Joint Disease, J. Bone & Joint Surg. **24**:858 (Oct.) 1926.

24. Hibbs, R. A., and von Lackum, H. L.: End-Results in the Treatment of Knee Joint Tuberculosis, J. A. M. A. **85**:1289 (Oct. 24) 1925.

25. Ely, L. W.: Further Observations on the Pathology of Joint Tuberculosis and Practical Deductions Therefrom, M. Rec. **78**:147 (July 23) 1910.

26. Friedrich, H.: Ueber Fehlerquellen der exakten Untersuchungsmethoden zum Nachweis von Tuberkulose und Aktinomykose, München. med. Wchnschr. **77**:1443 (Aug. 22) 1930.

In our group of 168 cases of proved tuberculosis, 75.6 per cent were correctly diagnosed clinically; in 13.6 per cent tuberculosis was considered as a possibility, and in 10.8 per cent the diagnosis of nontuberculous arthritis was made. Of the 66 cases of proved nontuberculous arthritis, 86.3 per cent were so diagnosed preoperatively, while 13.7 per cent were diagnosed as tuberculous.

Insidious onset, slow progress and frequent remissions and exacerbations point toward tuberculosis as the causative factor. Prolonged drainage from a joint without signs of acute inflammation is probably in favor of tuberculosis, but drainage itself is not diagnostic. In 11.3 per cent of our cases of tuberculosis there had been drainage for variable periods. It should be emphasized here that prolonged drainage in a case of tuberculosis usually means secondary infection, and such secondary infection, in most instances, so modifies the histologic picture as to make tuberculosis almost unrecognizable. Nineteen and seven-tenths per cent of patients without tuberculosis gave a history of drainage. Except in the cases of osteomyelitis with involvement of joints, the drainage of tuberculous material was more prolonged. The finding of tuberculosis elsewhere in the body may be helpful in the diagnosis. However, one of our patients had active pulmonary tuberculosis but the affected joint was not tuberculous. Ankylosis of bone demonstrated by the roentgen ray is definitely against tuberculosis, unless there has been secondary infection. Nevertheless, in many cases there are few clinical data for accurate differentiation.

The tuberculin test, although it has its enthusiastic proponents, cannot be considered a dependable diagnostic measure, especially if patients are adults. A negative reaction is of more significance as being against a diagnosis of tuberculosis. In 7.6 per cent of our nontuberculous cases, there was involvement of one other joint; in 21.2 per cent there was multiple involvement of joints, resembling that seen in the ordinary type of proliferative arthritis. In 13.1 per cent of the cases of tuberculosis one other joint was affected, while in 5.4 per cent mulitple joints were affected. Roentgenograms and specimens demonstrated the great difficulty of accurate diagnosis by the roentgen ray or by mere visualization at the time of exploration.

Inoculation of guinea-pigs is considered by many investigators to be an accurate diagnostic measure. The idea is not recent. Senn,[27] in 1887, quoted Tavel in the opinion that, when the distinction between tuberculosis and syphilis cannot be made clinically or by the microscope, inoculation experiments always give positive and reliable information. Recent

27. Senn, Nicholas: Four Months Among the Surgeons of Europe; A Series of Letters to Dr. Christian Fenger, Reprinted from J. A. M. A., 1887, vols. 8 and 9, Chicago, 1887.

opinions have varied as to the value of the procedure. Krause [28] stated: "The inoculations of guinea-pigs with suspected material for the diagnosis of tuberculosis should, in my opinion, rank as high in reliability as any laboratory procedure which we have." On the other hand, Smith,[29] in 1924, reported a series of 18 cases in which tuberculosis was found at the time of operation. Of these, the results of inoculation of guinea-pigs were positive in 10 and negative in 4. In 2 cases the pigs died too early for diagnosis, and in the remaining 2 the reports could not be traced. In a recent publication, Sundt [30] reported that in 25 per cent of his cases the results of inoculation of guinea-pigs were negative, but tuberculosis was found on microscopic examination of the tissue. In our cases, unfortunately, only 24 such inoculations were made. In 21 cases the results agreed with the microscopic data, 20 were positive and 1 was negative. In 3 cases the results of inoculation were negative, but the diagnosis of tuberculosis was made by examination of tissue. The error, therefore, in the results of inoculation of guinea-pigs was 12.5 per cent.

MICROSCOPIC DIAGNOSIS

There remains, then, the evaluation of microscopic examination as a method of diagnosis. Without doubt this method is not devoid of inaccuracy. At times there may be some contraindication to arthrotomy. Then again, as has been pointed out, the disease may be localized to one area of the joint, and unless generous and multiple specimens are sent to the laboratory the lesion may be overlooked. Furthermore, in cases of secondary infection it is extremely difficult to recognize the characteristic lesions, which appear greatly attenuated by the superimposed pathologic change and may even be entirely unrecognizable. It may be that in such cases inoculation of guinea-pigs will demonstrate what cannot be seen in the original tissue, but we had no opportunity to investigate this possibility.

In our series of 126 cases in which the pathologist diagnosed tuberculosis at the time of operation, we were able in every instance to confirm the diagnosis from examination of tissue of the preserved specimens, although in 22 cases additional sections were necessary in order to demonstrate the lesion. In the other 42 cases of this group microscopic sections were not made. Of the 66 nontuberculous specimens, 32 which had been so diagnosed at the time of operation were sectioned and reexamined; in 5 of these tuberculosis was definitely demonstrated.

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28. Krause, A. K., quoted by Ghormley.[23]

29. Smith, A. DeF.: The Early Diagnosis of Joint Tuberculosis, J. A. M. A. **83**:1569 (Nov. 15) 1924.

30. Sundt, Halfdan: The Diagnosis and Frequency of Tuberculous Disease of the Knee, J. Bone & Joint Surg. **29**:740 (Oct.) 1931.

Therefore, in the entire group of 158 microscopic sections, there was a pathologic diagnostic error of 3.2 per cent.

SUMMARY

The clinical history, roentgenograms, lesions discovered grossly and microscopically and results of inoculation of guinea-pigs in a series of 236 resections and 9 amputations of the knee joint have been studied.

The preoperative diagnosis was found to be incorrect in 24.4 per cent of the cases of tuberculosis and in 13.7 per cent of the cases of nontuberculous arthritis.

The gross specimens and roentgenograms were found to vary so widely as often to prevent the possibility of accurate diagnosis.

The inoculation of guinea-pigs proved incorrect in 12.5 per cent of the 24 cases in which inoculation was made.

The diagnosis made by microscopic examination of tissue removed at the time of operation has been found to be accurate in all but 3.2 per cent of the cases, an error of omission.

"ORBITAL INCLUSION" CYSTS AND CYSTO-ADENOMAS OF THE PAROTID SALIVARY GLANDS

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Cystic growths sometimes occur in the parotid salivary gland; they are lined with stratified epithelium, usually of the cylindric type, and rest on a base of lymphoid tissue. The latter is generally hyperplastic, and its growth either makes the lining appear papillated or, if it is extreme, fills the whole cyst with epithelial-clad lymphoid nodules. In the latter event the epithelium generally proliferates and forms small acini, and the growth assumes the pattern of a cystic adenoma. Sometimes, as in Cunningham's [1] case, the cysts are multiple. The epithelium is described by some authors as ciliated but more frequently as nonciliated. The cysts have appeared in persons of all ages from 12 to 74 years, have been twice as frequent in men as in women and are generally situated in the lower pole of the gland. Usually there are no symptoms except swelling with occasional twinges of pain unless there is infection. This can lead, as in other epithelial-lined cysts, to the formation of persistent sinuses. Removal of the cyst and all its lining will cure the condition.

The chief interest in these growths lies in the riddle of their origin. Although forming in adult life as a rule, it seems obvious that they must come from some developmental fault, for they are composed of tissues not found in the normally developed parotid gland.

We have had an opportunity to study three of these cysts—one reported by Cunningham,[1] one reported by Hanford [2] and one unpublished case. A perusal of published cases showed that there have been offered almost as many different explanations of their origin as there have been authors. This confusion led us to review the investigations of the embryology of the region of the anlage of the parotid gland, and

From the Surgical Pathological Laboratory of the College of Physicians and Surgeons, Columbia University, and the Surgical Department of the Presbyterian Hospital.

1. Cunningham, W. F.: Ann. Surg. **90**:114, 1929.

2. Hanford, J. M.: Branchiogenic Adenoma of the Neck, Ann. Surg. **94**:461, 1931.

as a result we have found, especially in the researches of Schulte,[3] what seems to be a satisfactory explanation for the cysts in a structure known as the "orbital inclusion." This gives rise to the orbital salivary glands in some of the carnivora and appears as a vestigial rudiment in human embryos.

REPORT OF CASES

CASE 1.—*History.*—R. M., a man, aged 61, a postoffice clerk, noticed a small mass at the angle of the left jaw for two years before coming to the hospital. It was entirely symptomless at first, but later gave slight twinges of pain. It did not interfere with mastication. Examination revealed an ovoid mass about 5 cm. in diameter directly over and somewhat behind the angle of the jaw. It was resilient but not definitely cystic. The skin was freely movable over it, but the mass was attached to the deeper structures. The patient also had a slight enlargement of the right lobe of the thyroid and suffered from chronic myocarditis and emphysema.

Operation (Aug. 15, 1930, by Dr. John M. Hanford [2]).—With the patient under intranasal ether anesthesia, a curved incision 6 cm. long was made from the lobe of the ear downward and forward exposing the tumor in the parotid region. It was well encapsulated and was removed by sharp and blunt dissection. When the tumor was removed from the anterior portion two or three drops of what appeared to be pus escaped, but no abscess cavity was found. One goiter tube drain was inserted.

Course.—The wound drained purulent exudate for six days. Staphylococcus albus was obtained on culture. The patient was discharged the seventh day with slight induration about the wound. No evidence of infection was present after two weeks. After seven months there was apparently no reappearance of the lesion.

CASE 2.—*History.*—D. L., a woman, aged 74, had noticed a small tumor below and in front of the left ear four years before coming to the clinic. Two years later it began to grow noticeably larger and to extend backward. During this time it had given no symptoms and did not interfere with mastication. Examination revealed a fusiform tumor mass at the angle of the jaw measuring approximately 6 by 4 cm. It extended backward, elevating the lobe of the ear. It was thought to be fluctuant and was freely movable in the subcutaneous tissue. No other significant findings were present. Roentgen examination of the parotid region showed no evidence of calcification or of a calculus.

Operation (April 24, 1928, by Dr. W. Barclay Parsons, Jr.).—With the patient under ethylene anesthesia, a curved incision was made and carried down to the wall of the cyst which was well encapsulated, lying in the substance of the parotid, but not apparently associated with the duct system. The cyst ruptured, with an escape of creamy material, allowing it to be enucleated with ease. An iodoform gauze drain was inserted.

Course.—The drain was slowly withdrawn, drainage being slight, and in one week the wound was completely healed. Three years later there was no evidence of reappearance.

PATHOLOGIC EXAMINATION

At operation it was noted that both of these tumors were within the substance of the lower pole of the parotid gland, but were distinctly encapsulated and separated from the salivary tissue.

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3. v. Schulte, H. W.: Studies in Cancer and Allied Subjects: II. The Development of the Human Salivary Glands, New York, Columbia University Press, 1913, vol. 4.

Macroscopic Examination.—The tumor from the first case was a rather firm, lobulated mass measuring 4 by 3.5 by 3 cm. Externally it was covered with a smooth capsule to which no appreciable parotid tissue was adherent. Cross-section through the central part of the tumor (fig. 1) showed irregular wide trabeculae of soft grayish tissue separated by masses of yellowish material. This has been

Fig. 1 (case 1).—Cross-section through the mass removed.

Fig. 2 (case 2).—The cystic mass cut open to show the papillary lining.

removed in some places, showing narrow clefts, but no large cystic acreas were present.

In the second case the specimen was distinctly a cystic structure measuring 3 cm. in diameter. The capsule was smooth, and on cut section the wall consisted of rather firm white tissue on the inner surface of which were small rounded elevations varying from 1 to 2 mm. in diameter (fig. 2).

Microscopic Examination.—In case 1, the tumor was composed of irregular masses of lymphoid tissue covered with epithelial cells. These were so arranged

that in some instances glandlike spaces were formed, while elsewhere there were dilated spaces filled with granular cellular débris (fig. 3). The epithelial layers were from three to four cells thick, the cells varying from cuboidal to a low cylindric shape. Masson's trichrome stain showed that the cytoplasm of the more

Fig. 3 (case 1).—Photomicrograph showing a dilated space filled with débris into which project masses of lymphoid tissue clothed with epithelium. At the left is a group of epithelial glands.

superficial cells contained acidophilic granules which were absent in the cells of the deeper layers. With the mucicarmine stain, occasional vacuoles filled with mucin were demonstrated in some epithelial cells. None of the surface cells was ciliated (fig. 4). The whole mass was enclosed within a thin fibrous capsule and supported by slender fibrous trabeculae.

In case 2, the walls of the cyst were lined with stratified cylindric epithelium similar to that in the first case. The nodular effect was caused by the hyperplastic lymphoid follicles which lay between the epithelial lining cells and the fibrous capsule (fig. 5). The epithelial lining cells were not ciliated and contained the same droplets of mucus and superficial acidophilic granules (fig. 6) as were noted in the first case.

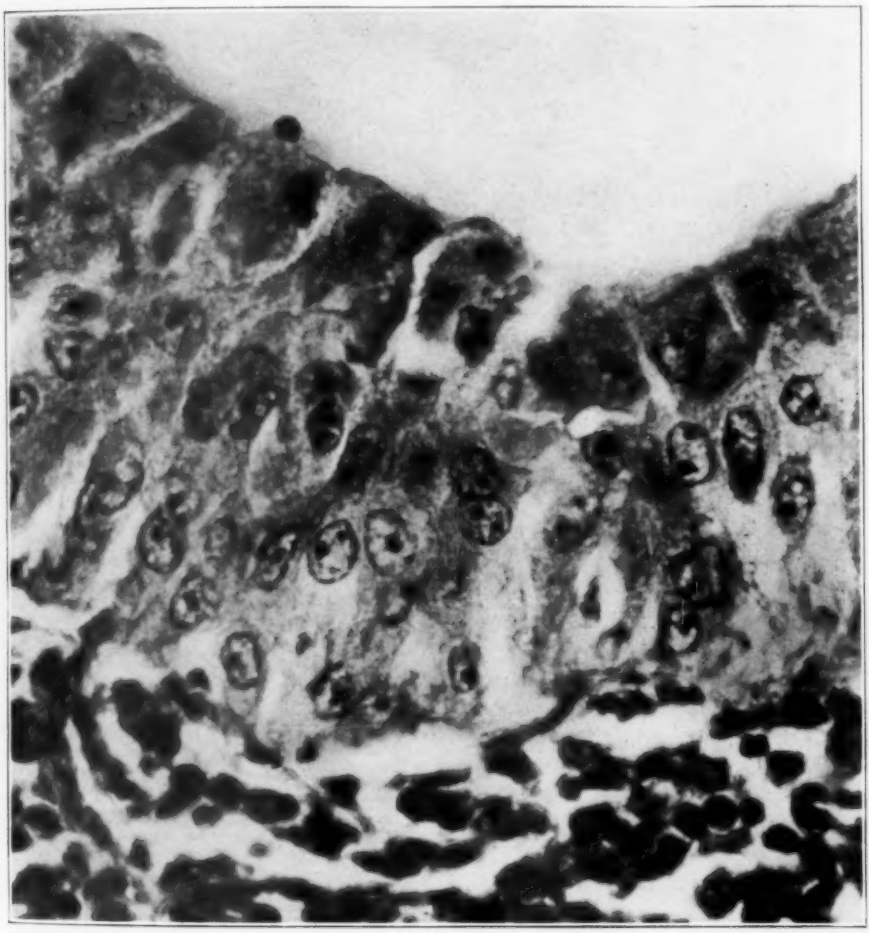


Fig. 4 (case 1).—Detail photomicrograph showing the stratified cylindric epithelium resting on lymphoid cells. The darker granules in the cytoplasm of the superficial layer of epithelial cells are acidophilic.

ETIOLOGY

In the accompanying table will be found listed all of the cystic growths of the parotid with an epithelial lining and lymphoid tissue of which we have been able to find records. It includes a summary of

Summary of Previously Reported Cases

Observer	Sex	Age	Location of Tumor	Pathology	Interpretation
Hildebrant: Arch. f. klin. Chir. **49**: 167, 1898	M	41	Left angle of jaw in parotid region	Flattened and ciliated epithelium covering lymphoid tissue showing germinal centers	Mentioned in report of 20 cysts and fistulas of the neck; all considered of branchiogenic origin
Sultan: Deutsche Ztschr. f. Chir. **48**: 143, 1898	M	44	Extending from left ear to masseter muscle	Stratified ciliated or columnar epithelium forming projections in lymphoid tissue	Mentioned in report of 22 cysts of parotid
Morestin: Bull. Soc. anat. de Paris **4**: 709, 1902	F	23	Right posterior parotid region elevating ear	Stratified squamous epithelium; deeper cells polyhedral	Not similar to parotid glandular epithelium but derived from evagination of embryonal buccal ectoderm
Lecène: Rev. de chir. **37**: 1, 1908	F M	40 50	Right parotid region	Adenoma of stratified and ciliated epithelium	Similar to embryonic tonsil; derived from pharyngeal ectoderm in region of third or fourth branchial pouch
Albrecht and Artz: Frankfurt. Ztschr. f. Path. **4**: 47, 1910	M F	64 12	Left parotid Right parotid	Both cystadenomas consisting of lymphoid tissue with follicles lined by high columnar nonciliated epithelium	(1) Changes in endothelium of lymph glands; (2) heterogenic epithelium derived from pharynx included in lymph gland; (3) from anlage of salivary duct epithelium
Glass: Frankfurt. Ztschr. f. Path. **9**: 335, 1912	M	65	Left angle of jaw	High cylindric epithelium containing eosinophilic granules resting on lymphoid tissue	Included epithelium in lymphoid tissue as cervical sinus closes
Delanglade, Peyron and Rouslacroix: Bull. Assoc. franç. p. l'étude du cancer **7**: 370, 1914	F	33	Left parotid lower pole	Cylindric epithelium covering lymphoid tissue containing masses of concentric squamous epithelial cells	Similar to Hassall's corpuscles and possibly derived from thymus
Menetrier, Peyron and Surmont: Bull. Assoc. franç. p. l'étude du cancer **12**: 205, 1923	M	50	Parotid	Single or double layer of high columnar epithelium in some places ciliated. These rest on lymphoid tissue containing follicles	Parabranchial cyst not derived from branchial cleft; possibility of embryonal rest of undifferentiated salivary structures (Neisse: Anat. Hefte **10**: 287, 1898)
Mazza and Cassinelli: Rev. Asoc. méd. argent. **35**: 317, 1923	M	36	Left parotid	Ciliated columnar epithelium with lymphoid tissue	Branchiogenic cystadenoma similar to those of Albrecht and Artz
Rikl: Zentralbl. f. allg. Path. u. path. Anat. **35**: 310, 1924-1925	M	47	Right parotid	High cylindric epithelium in lymphoid tissue	Cellular inclusion by lymphoid tissue within the parotid gland as it develops
Askanazy, quoted by Sternburg in Henke and Lubarsch: Handb. d. spez. path. Anat. u. Histol., Berlin, Springer, 1926, pt. 1, vol. 1, p. 331; also by Lang, ibid., 1929, pt. 5, vol. 2, p. 127	M	54	Left parotid	Stratified cuboidal epithelium included in lymphoid tissue showing follicles	Reported in Lubarsch's textbook; some previous theories mentioned
Houdard and Hufnagel: Bull. Assoc. franç. p. l'étude du cancer **16**: 377, 1927	M	58	Parotid	Cystic tumor lined by high cylindric epithelium with lymphoid tissue showing germinal centers	Some previous theories reviewed
Spitznagel: Zentralbl. f. allg. Path. u. path. Anat. **46**: 282, 1929	M M	65 45	Left parotid Lower pole of left parotid	High cylindric epithelium resting on lymphoid tissue	Similar to that of Albrecht and Artz
Warthin: J. Cancer Research **13**: 116, 1929	M	60	Left parotid	Ciliated stratified columnar epithelium resting on lymphoid tissue	Similar to polyps of eustachian tube and represent developmental disturbance of eustachian tube anlage
Cunningham: Ann. Surg. **90**: 114, 1929	M	16	Right parotid	Stratified cylindric epithelium resting on lymphoid tissue	Branchiogenic origin
Hanford: Ann. Surg. **94**: 461, 1931	M	61	Lower pole of left parotid	Stratified cylindric epithelium resting on lymphoid tissue	Branchiogenic origin

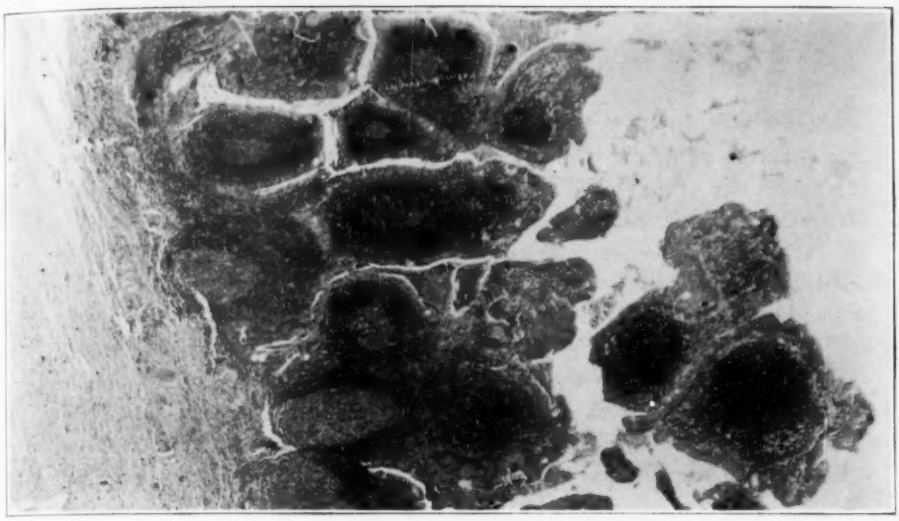


Fig. 5 (case 2).—Photomicrograph showing that the papillary projections pictured in figure 2 are made up of lymphoid tissue clothed with epithelium.

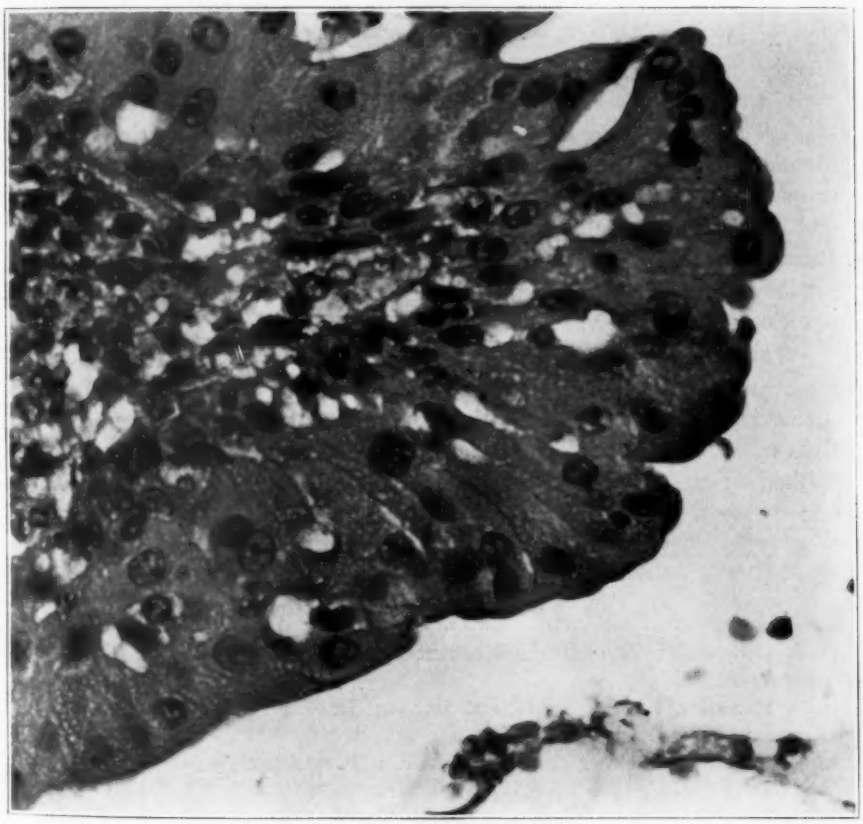


Fig. 6 (case 2).—Detail photomicrograph showing the stratified cylindric epithelial lining resting on lymphoid tissue.

each author's interpretation of the origin of the cyst. Every writer recognized that neither the epithelial lining nor the lymphoid tissue was characteristic of the adult parotid and supposed that it must have come from some developmental aberration.

The earliest writer, Hildebrant,[4] mentioned his case in connection with the report of a group of branchial cysts of the neck and apparently thought it had the same origin. Morestin,[5] in 1902, suggested that these cysts must have been derived from evaginations of the embryonal buccal ectoderm within the parotid gland as it developed, although he did not support it with convincing embryologic and phylogenetic evidence. As will be shown later, this is the probable derivation, but Morestin was unfamiliar with the mechanism of their formation. The similarity of the epithelium to that of the pharynx and its close association with lymphoid tissue led Lecène[6] to suppose that the growth represented the development of an ectopic tonsil, and he traced its elements to an inclusion of a portion of the pharyngeal ectoderm in the region of the third or fourth branchial pouch. Glass[7] supposed the inclusion of a few pharyngeal ectodermal cells as the cervical sinus closes. Delanglade, Peyron and Rouslacroix[8] found a somewhat similar growth in the carotid region and reported it at the same time as their parotid cyst. They saw some concentrically arranged cells resembling Hassall's corpuscles, and they supposed a separation of a portion of the thymic anlage. Menetrier, Peyron and Surmont[9] studied Neisse's[10] drawings of the embryonal parotid tissue which show lymphoid tissue and epithelium resembling that found in the cysts. They therefore suggested that these tumors might be remnants of undifferentiated salivary structures which did not fuse with the duct system of the parotid but grew later as segregated tumors.

Warthin[11] studied a case in which the tumor was lined with ciliated epithelium. He noted a resemblance to some of the polyps of the eustachian tube and concluded that these parotid cysts might be derivatives of the first branchial pouch and cleft. He does not tell how this epithelium could be enclosed within the parotid. The other hypotheses

4. Hildebrant, O.: Arch. f. klin. Chir. **49**:167, 1898.

5. Morestin: Bull. Soc. anat. de Paris **4**:709, 1902.

6. Lecène, P.: Rév. de chir. **37**:1, 1908.

7. Glass, E.: Frankfurt. Ztschr. f. Path. **9**:335, 1912.

8. Delanglade; Peyron, and Rouslacroix: Bull. Assoc. franç. p. l'étude du cancer **7**:370, 1914.

9. Menetrier, P.; Peyron, A., and Surmont, J.: Bull. Assoc. franç. p. l'étude du cancer **12**:205, 1923.

10. Neisse, R.: Ueber den Einschluss von Parotsläppchen in Lymphknoten, Anat. Hefte **10**:287, 1898.

11. Warthin, A. S.: J. Cancer Research **13**:116, 1929.

included in the list do not seem to us to have sufficient credibility to warrant serious discussion.

All of these writers, then, believe that these cystic growths are derivatives of either the branchial pouch or the cleft epithelium, of the buccal or pharyngeal ectoderm other than that from which the parotid is developed or from segregated cells of the parotid anlage itself.

A brief review of the development and metamorphosis of the branchial system will make it clear that there is no embryologic basis for supposing that parotid cysts could represent developments from its remnants. In early embryonic life there are four external branchial arches separated by depressions or clefts externally and by pouches internally.[12] The clefts and the pouches are not continuous but are

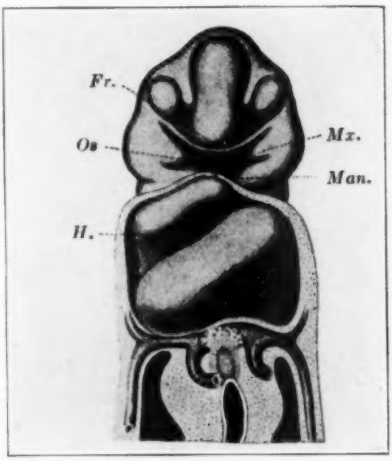


Fig. 7.—Ventral view of the anterior portion of an embryo of 2.15 mm., from a reconstruction (His). *Fr.* indicate frontal process; *H.*, heart; *Mx.*, maxillary process; *Man.*, mandibular process; *Os*, oral sinus. (Figures 7 and 8 are from Keibel and Mall: Human Embryology, Philadelphia, J. B. Lippincott Company.)

separated by a thin membrane covered by ectoderm on the outer surface and by entoderm on the inner surface. The first and second arches develop out of proportion to the third and fourth which they overlap, producing a deep depression called the cervical sinus.[13] It is supposed that a majority at least of the branchial cysts and fistulas in the neck develop from this structure.[14] These develop below the second or

12. Bailey and Miller: Textbook of Human Embryology, ed. 2, New York, William Wood & Company, 1911.

13. Semken, G. H.: Embryology of Branchiogenetic Cysts and Fistulae, in Nelson Loose-Leaf Living Surgery, New York, T. Nelson & Sons, 1927, vol. 2, p. 783.

14. Wood, F. C.: Branchiogenetic and Other Congenital Cysts, in Nelson Loose-Leaf Living Surgery, New York, T. Nelson & Sons, 1927, vol. 2, p. 113. Keith, A.: Congenital Malformations of Palate, Face and Neck, Brit. M. J. **2**:438, 1909.

hyoid arch.[15] The first pouch and cleft form the eustachian tube and the external auditory canal and are separated by the membrana tympani. Since the parotid gland does not come into intimate relationship with any of these structures, it is difficult to understand how portions of them can be included within its substance. For this reason we have rejected the branchial hypotheses.

In order to discuss the possibilities of the remaining hypotheses that have to do with the segregation of some cells of the parotid anlage or of the oral ectoderm, the embryology of this region must be described. The first branchial arch divides into upper and lower portions.[16] The upper or maxillary portion is divided by the two nasal pits into a

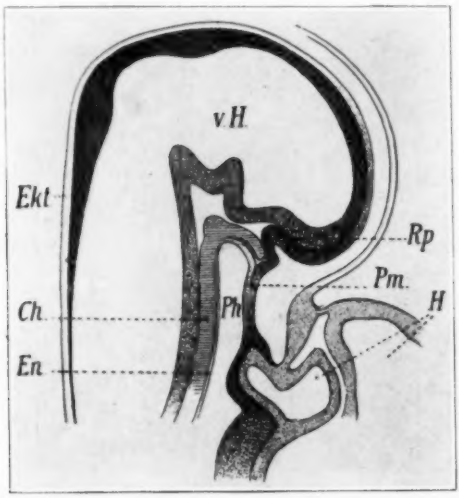


Fig. 8.—Median longitudinal section of a rabbit embryo. *Ch.* indicates chorda; *Ekt.*, ectoderm; *En.*, endoderm; *H.*, heart; *Rp.*, Rathke's pouch; *Ph.*, pharynx; *Pm.*, pharyngeal membrane; *v.H.*, forebrain.

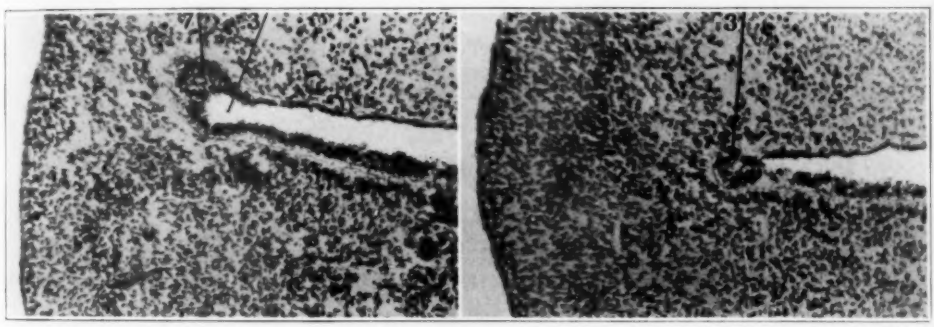
medial portion giving rise to the lips and a lateral portion from which the cheek is formed. The lower portion of the first branchial arch forms the mandible. The primitive oral sinus is pentagonal, having for its boundaries laterally the maxilla and mandible and superiorly the frontal process of the brain, while inferiorly it is separated from the pericardium by a thin membrane (fig. 7). In a 2 mm. embryo the floor of the oral sinus is formed by a membrane which separates it from the pharynx. This is lined on the oral side by ectoderm and on the pharyngeal side

15. Carp, L., and Stout, A. P.: Branchial Anomalies and Neoplasms, Ann. Surg. **81**:186, 1928.

16. McMurrich, J. P., in Keibel and Mall: Human Embryology, Philadelphia, J. B. Lippincott Company, 1912, vol. 7, p. 335.

by entoderm (fig. 8). In the 2.5 mm. stage this membrane has disappeared and the oral sinus and pharyngeal cavity are continuous, leaving as a remnant only a transverse ridge immediately posterior to Rathke's pouch. The lateral and superior lining of the buccal cavity therefore is derived from ectoderm. The floor of the mouth and the tongue are derived from three sources: (1) the tuberculum impar anteriorly, formed by the fusion of the mandibles; (2) the lateral portions, formed from the fusion of the second branchial arches, and (3) the base or copula, formed from the medial expansions of the third and fourth branchial arches.

In the lateral recess of the oral cavity there is a sulcus which extends from the angulus oris to the opening of the first pharyngeal pouch. Schulte [3] called this the buccal sulcus. In embryos of 8 mm. there is a slight thickening of the epithelium along the fundus of this sulcus near the angulus oris (fig. 9 *A*). This is the anlage of the parotid



A B

Fig. 9.—*A*, transverse frontal section of the buccal sulcus near the angulus oris of a 20 mm. human embryo. The first evidence of beginning parotid development is a thickening of the epithelium of the buccal sulcus (*7*). *B*, transverse section of the buccal sulcus more caudad than *A*, showing the epithelial thickening (*3*) which gives rise to the orbital inclusion. (Figures 9 to 12 are from Schulte: Studies in Cancer and Allied Subjects: II. The Development of the Human Salivary Glands, New York, Columbia University Press, 1913, vol. 4.)

gland. Further thickening occurs until a flange of epithelium develops which grows backward (fig. 10, *2*) through the mesenchyme of the cheek crossing the internal surface of the masseter and pterygoid muscles until it reaches the neighborhood of the external ear. This flange becomes canalized, and sprouts develop from it. By a continuation of this process of sprouting the embryonal gland eventually comes to assume its adult form.

In the past there have been described what seemed to be accessory parotid anlages, and those who observed them supposed that they were derived from the parotid duct. In the series of observations made by

Weishaupt,[17] the hypothesis was advanced that these structures became separated from the parotid duct system and remained vestigial. If this observation is correct there would be strong grounds for supposing that such vestigial segregated closed tubular structures might be the origin of cysts. For this reason we shall review these observations in some detail.

In 1885, Chievitz [18] reported that he found in a 9 to 10 week human embryo a small solid branch of cells given off superiorly from the

Fig. 10.—Transverse section of a 20 mm. human embryo showing the separation of the parotid anlage from the buccal sulcus; *2*, parotid anlage; *13*, postglandular flange; *14*, alveolar sulcus; *16*, intermediate sulcus; *21*, Meckel's cartilage; *28*, superior dental anlage; *30*, lingual nerve; *34*, ectopalatine sulcus; *38*, orbitoparotid.

parotid duct as it passed along the masseter muscle. In a 12 week embryo he found a similar structure which arose from the parotid duct and had a course about 1 mm. long from the masseter to the pterygoid

17. Weishaupt, Elizabeth: Ein rudimentärer Seitengang des Ductus Parotideus, Arch. f. Anat. u. Entwcklngsgesch., 1911, p. 11.

18. Chievitz, J. H.: Beiträge zur Entwickelungsgeschichte der Speicheldrüsen, Arch. f. Anat. u. Entwcklngsgesch., 1885, p. 401.

where it ended blindly. It was lined with epithelial cells with oblong nuclei arranged about a lumen. Chievitz considered this structure an accessory parotid.

In 1911, Elizabeth Weishaupt [17] described an embryonic structure that she found on both sides in twenty of twenty-four human embryos and on one side in one of the other four. This was a blind tube, not connected with the ductus parotidis, which lay near the duct between the mucous membrane of the buccal sulcus and the anterior border of the masseter muscle. It was smaller than the normal ductus parotidis, lined with epithelium and surrounded by the mesenchymal tissue. In one

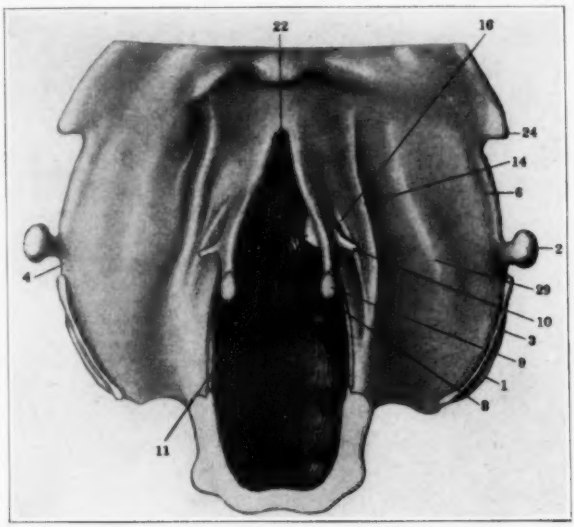


Fig. 11.—Reconstruction of the oral epithelium of a 20 mm. human embryo; ventral view showing the relation of the orbital inclusion to the parotid gland anlage: *1*, buccal sulcus; *2*, parotid anlage; *3*, orbital inclusion; *4*, orbitoparotid interval; *6*, proparotid ridge; *8*, lingual sulcus; *9*, submaxillary anlage; *10*, greater sublingual gland; *11*, anlage of apical gland; *14*, alveolar sulcus; *16*, intermediate sulcus; *22*, frenulum; *24*, angulus oris; *29*, inferior dental anlage.

24 mm. human embryo it was cystic at both ends, the lumens being lined with flattened cells which in some places were forced in toward the center of the lumen. This structure she called the "ramus mandibularis" of the parotid duct. She expressed the belief that it is vestigial in man and is not developed into any adult structure. In mammals she supposed that it represented the anlage of the dorsal and ventral buccal glands. Weishaupt and McMurrich,[16] who also observed this structure in human embryos of 9 weeks and earlier, remarked that

its significance was unknown in human beings, but that since it was a tube with blind ends it might give rise to cysts.

It is obvious that Chievitz and Weishaupt described the same structure, and that its vestigial tubular character favors the development of cysts. Were they correct in their hypothesis that it was derived from the anlage of the parotid, then we should agree with Menetrier, Peyron and Surmont [9] that the cysts came from segregated embryonal parotid gland.

Fig. 12.—Transverse section of a 20 mm. human embryo through the buccal sulcus, more caudad than in figure 10, showing the orbital inclusion separated from the sulcus: *1*, buccal sulcus; *3*, orbital inclusion; *33*, buccal nerve.

However, the investigations of Schulte,[3] Huntington [19] and Carmalt [20] into the development and comparative anatomy of the whole salivary

19. Huntington, George S.: Studies in Cancer and Allied Subjects: III. The Anatomy of the Salivary Glands in the Lower Primates, New York, Columbia University Press, 1913.

20. Carmalt, Churchill: Studies in Cancer and Allied Subjects: V. The Anatomy of the Salivary Glands in the Carnivora, New York, Columbia University Press, 1913.

system, published in 1913, showed conclusively that the structure described by Chievitz and Weishaupt has a different origin and is not part of the parotid anlage. Schulte [3] showed that in human embryos of from 9 to 10 mm. there occurs a continuous thickening along the fundus of the buccal sulcus posterior to the anlage of the parotid and separated from it (fig. 11, *3*). Out of this continuous anlage, a cylinder of cells is formed by a process of folding and constriction (fig. 9 *B*). Ultimately this group of cells is widely displaced laterad from the oral ectoderm (fig. 12, *3*) and comes to lie in close contact with the ental surface of the muscles of mastication. This structure Schulte calls the orbital inclusion and identifies it with those described by Chievitz and Weishaupt. He explains Chievitz' observation of a communication with the parotid duct near its outlet in the buccal sulcus by saying that sometimes there is no orbitoparotid interval between the parotid anlage and the orbital inclusion, and in such case a development from the orbitoparotid (fig. 11, *4*) might be attached to the parotid duct. As the parotid gland increases in size it approaches nearer and nearer to the orbital inclusion until, finally, in embryos of 12 weeks they lie in contact with one another. The subsequent fate of the orbital inclusion in man has never been investigated, but in the cat, dog and some other carnivora it forms the orbital glands. These are salivary glands which are embedded in the infra-orbital fat. Their ducts, according to Carmalt,[20] open on a low stomal ridge opposite and behind the upper molars.[21]

In man, therefore, the orbital inclusion is a vestigial closed tubular structure, lined with ectodermal epithelium which lies in contact with the lower portion of the parotid gland. It is well known that closed tubular vestiges in other parts of the body may form cysts in adult life. Weishaupt [17] recorded microscopic cystic dilatation of one of the orbital inclusions that she studied. For these reasons it seems fair to assume that the probable origin of these lympho-epithelial cysts of the matured parotid is from a dilatation and proliferation of the orbital inclusion.

21. Carmalt (footnote 20) described a series of orbital glands in man which are situated in series with the superior alveobuccal glands but behind the opening of the parotid duct. These are not developed from the parotid duct but probably from the orbitoparotid interval. Other authors have called them malar glands.

PRESERVED FASCIA IN HERNIA REPAIR

WITH SPECIAL REFERENCE TO LARGE POSTOPERATIVE HERNIAS

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BALTIMORE

During the last decade there have been many innovations in the operations for the various types of hernia, as regards both the technic of the operations themselves and the materials used in the repair. My object in this paper is to discuss briefly, in general, the use of fascia strips, with especial reference to the preserved material, and then to discuss specifically the application of the method to one of the most difficult problems in hernia, namely, large postoperative hernias.

Gallie and LeMesurier,[1] in recent years, have extensively employed autogenous fascia lata in the repair of hernial defects. They have largely used strips of fascia lata, either as an ordinary suture material to approximate the edges of hernial defects, or, in gaps, the edges of which cannot be approximated, as a basketweave network to close the defects. They have shown experimentally that such transplants persist as living tissues and become incorporated into the tissues among which they are transplanted as an integral part of the organism. They constitute, therefore, not merely an additional suture material, but, in addition, perform all the functions of grafts. They form a most noteworthy contribution to the surgical armamentarium.

I [2] have shown that animal fascia preserved in alcohol may be used in exactly the same way as living fascia taken from the thigh of the patient that is being operated on (figs. 1 and 2). This avoids the necessity of performing an extra operation in order to get the material needed to repair the hernial defect. Briefly, the underlying principles in the use of alcohol-preserved animal fascia may be stated as follows: The collagen fibrils of the connective tissues are inert, intercellular substances, and have no life in the sense that living protoplasm has life. These fibrils are not altered chemically or physically by being preserved in alcohol. When implanted in a living organism among their fellows

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From the Department of Surgery of the Johns Hopkins Medical School.

Read before the Travis County Medical Society, Austin, Texas, Nov. 17, 1931.

1. Gallie, W. E., and LeMesurier, A. B.: The Transplantation of the Fibrous Tissues in the Repair of Anatomical Defects, Brit. J. Surg. **12**:289 (Oct.) 1924.

2. Koontz, A. R.: Experimental Results in the Use of Dead Fascia Grafts for Hernia Repair, Ann. Surg. **83**:523 (April) 1926.

of the same kind (after being thoroughly washed in salt solution), one would not then expect them to produce a foreign body reaction, induce phagocytosis or show a tendency to be absorbed. They are like the tissues among which they have been implanted, both chemically and physically, and it has been shown experimentally that living cells wander in among the inert fibers, new fibroblasts grow in between them, and in a short time the implanted material is incorporated with the tissues of the host as permanent living material. The reason that catgut

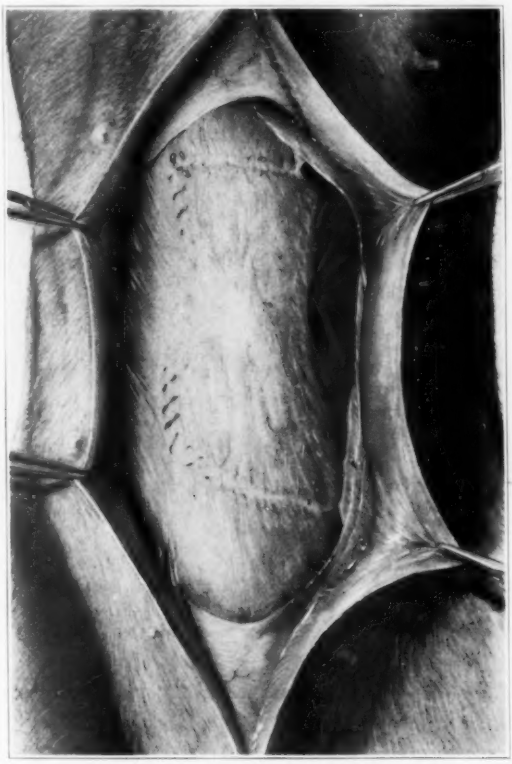

Fig. 1.—Repair of large ventral hernia in an animal with a piece of alcohol-preserved ox fascia lata; five months after operation.

and kangaroo tendons do not act in the same way is that the collagen fibrils of these materials are altered both chemically and physically in the process of their preparation. Various chemicals, such as chromic acid, are used, and they are also heated in the process of preparation. Besides, their strands are generally so twisted and hardened that it would be impossible for fibroblasts from the surrounding tissues to grow into them, even if there were no question of a complicating chemical and physical alteration of the fibrous framework.

Since the publication of my first work on dead fascia grafts, strips of alcohol-preserved fascia have come to be widely used in the repair of hernial defects. This material has been used in other operations, such as those of habitual dislocation of the shoulder, repair of the sphincter ani in cases of fecal incontinence, open reduction of fractures, etc. My experimental results and conclusions as to the fate of alcohol-preserved fascia have been confirmed experimentally by Rosenblatt and Meyers [3] of Detroit, McNealy and Lichtenstein [4] of Northwestern University, and Horsley [5] of Richmond. Also, Wolfsohn [6] has shown that strips of fascia preserved in a solution of 1 part formaldehyde and 100 parts of alcohol, after implantation in animals, retain their tensile strength for as long as twenty-one months, which was as long as obser-

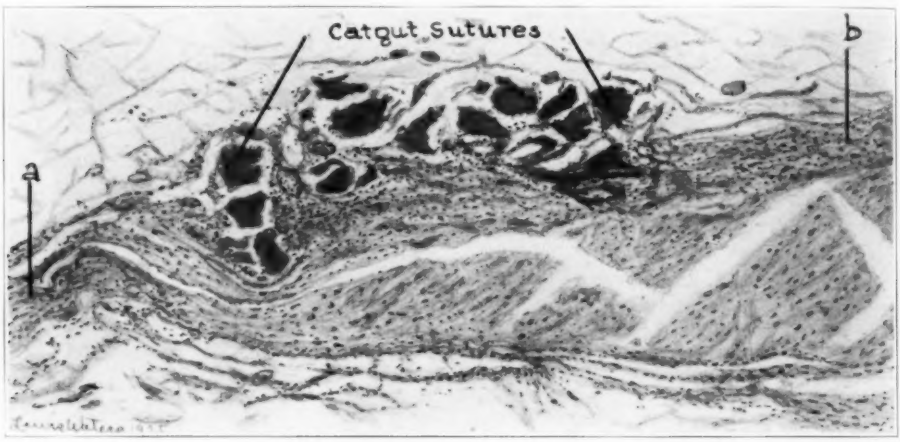

Fig. 2.—Microscopic drawing showing union of preserved and living fascia four months after operation: *a*, living fascia of host; *b*, dead graft.

vations were made. Besides, numerous other European investigators have confirmed the original work of Nageotte as to the fate of preserved tendons when implanted in animals. As the connective tissues of tendon and fascia are so nearly related, it is to be presumed that the behavior of these materials when implanted would be similar. Some workers

3. Rosenblatt, M. S., and Meyers, M.: Muscle-Fascia Suture with Preserved Fascia and Tendon, Surg., Gynec. & Obst. **47**:836 (Dec.) 1928.

4. McNealy, R. W., and Lichtenstein, M. E.: A Study of the Use of Fascial Grafts, Illinois M. J. **56**:140 (Aug.) 1929.

5. Horsley, G. W.: The Behavior of Alcohol-Preserved Fascia Lata of the Ox, Autogeneous Fascia and Chromicized Kangaroo Tendon in Dog and in Man, Ann. Surg. **94**: 410 (Sept.) 1931.

6. Wolfsohn, G.: Ueber die Verwendung von tierischen Fascienfäden, Arch. f. klin. Chir. **147**:479 (Oct. 15) 1927.

claim that when these tissues are implanted there is a substitution of fibers from the host for the implanted fibers. Others claim that the implanted fibers remain intact and function as a part of the host. This question is a matter of academic interest, but of no real practical importance. It matters little whether the implanted material functions as originally implanted, or by the use of fibers borrowed from the host. The point of practical interest is that the implant does function.

Horsley's article [5] contains some rather surprising conclusions. After reporting his experiments, which confirmed mine as to the fate in dogs of alcohol-preserved ox fascia lata, he stated that "from clinical experience the reactions of this alcohol-preserved fascia lata of the ox in man have been contrary to what would be expected from these experiments in dogs." This conclusion is based almost entirely on two human operative cases, one a pyloroplasty and the other a gastro-enterostomy, in which the abdominal wounds were closed in layers, catgut being used throughout, except in the anterior sheath of the rectus, which was closed with a continuous suture of alcohol-preserved ox fascia lata. Within ten days after operation both wounds broke open. It seems to me that Horsley's conclusions that alcohol-preserved fascia behaves differently in man and in the dog is based on insufficient evidence. I have discussed this in detail elsewhere.[7] I do not believe that fascia should be used in closing the wound after operations on the stomach, owing to the action of the digestive juices on the fascia.

The fact that myself [8] and many other surgeons have used alcohol-preserved ox fascia lata successfully in repairing difficult hernia shows that the material does remain intact in man for a considerable length of time, at least long enough to effect cures in cases in which other methods have failed. I have used the material in eighty-five operations for hernias of all sorts, many of which were difficult and were referred to me only because it was felt that they were hopeless as to cure, but that it would do no harm to try a fascial repair. In spite of the large number of difficult cases, I know of only three recurrences. I will cite only one case, which seems to me ample proof that preserved fascia persists in man just as it has been shown experimentally to persist in dogs. This case was that of a man, aged 70, who had been operated on five times before for a left inguinal hernia. Each time the hernia had recurred within a month or two after operation. The patient was referred to me by the surgeon who had operated on him the fifth time, and who felt that the hernia could not be cured by the usual methods.

7. Koontz, A. R.: Suture Material for Hernia Repair, with Special Reference to Preserved Fascia Strips, South. M. J. **25**:372 (April) 1932.

8. Koontz, A. R.: Dead (Preserved) Fascia Grafts for Hernia Repair: Clinical Results, J. A. M. A. **89**:1230 (Oct. 8) 1927; New Principles and Procedures in Hernia Repair, Texas State J. Med. **24**:259 (Aug.) 1928.

He had a scrotal hernia about the size of a cocoanut, which could not be reduced when he was examined at my office. At operation an enormous amount of dense scar tissue was encountered, but the different layers were dissected out as well as possible. The sac contained several loops of intestine which were adherent to its wall. The neck of the sac was 3 inches (7.6 cm.) in diameter. After the sac had been dissected free and excised, the peritoneal opening was closed with a running suture of fine black silk. The hernia was then repaired with alcohol-preserved ox fascia lata strips, making a basketweave according to the Gallie technic. It has now been more than five years since this patient was operated on, and there has not been the slightest evidence of a recurrence. Many other such examples could be cited.

A rather striking example of the efficacy of the material is found in the recent report of Stone [9] on the voluntary control of incontinent anal sphincters by the use of double loops of fascia lata encircling the anus and a portion of the gluteus muscles. Here the control is entirely dependent on the loops of fascia constricting the anus through voluntary contracture of the gluteus muscles. Stone has reported eleven cases in which this method was used, with nine good and two poor results. In four of the successful cases, strips of alcohol-preserved fascia were used. Naturally, if the fascia were absorbed soon after implantation, these patients would have lost anal control. The fact that the patients have now maintained anal control for two years or more after operation is positive proof that the fascia is still functioning. This is a striking clinical example of the usefulness of the material. It matters little whether the original strands of ox fascia are still present in these persons, or whether they have been replaced by fibers from the host. The functional result is the same.

LARGE POSTOPERATIVE HERNIAS

Small postoperative hernias often present one of the easiest problems in major surgery, and are usually easy to cure by any careful procedure that the surgeon may select. On the other hand, large postoperative hernias are extremely difficult to cure, and often present one of the most troublesome problems that the surgeon has to confront. Of course, the ideal way to treat a large postoperative hernia is to operate when it is small and the operation is easy. There is a much larger proportion of large hernias in this group than in any other group. Some postoperative hernias are large from the beginning, owing to a general breaking down of the operative incision. This type usually develops soon after operation, and may develop while the patient is

9. Stone, H. B.: Plastic Operation to Restore Voluntary Anal Control, J. A. M. A. **97**:1205 (Oct. 24) 1931.

still in bed. In another group, the hernia is small to begin with and may remain so for years. However, once it starts to enlarge the progress is fairly rapid, owing to the nonresisting nature of the soft parts surrounding the hernia. The muscles and fascia are often thinned out and weakened, and yield readily to the constant force of intra-abdominal pressure exerted against them. The large hernias generally cause rather severe symptoms, such as an uncomfortable sense of weakness in the abdominal wall, dragging down pain, digestive disturbances, constipation and inability to engage in any sort of strenuous work. Some of the hernias become so large as to incapacitate the patient completely. I recently operated on one so large that an abdominal support was no longer of much help, and about the only way the patient could lead an even moderately comfortable life was to sit around and hold his abdominal contents back with his hands. However, the presence of a postoperative hernia should not preclude the surgeon from thinking of a concomitant condition which might be responsible for the patient's symptoms, such as gastric or duodenal ulcer, colecystitis or colelithiasis and kidney or ureteral stone. Patients suffering with these conditions have been operated on for hernia, with a cure of the hernia, but, naturally, without relief of symptoms, when the symptoms were due to some other condition.

A good many large, postoperative hernias occur in obese persons. In fact, obesity is an important etiologic factor in their production. Before operating on such patients, rigid dietary measures should be introduced in an effort to reduce their weight. A great deal of the excess weight of obese persons is carried in the omentum, and a reduction of this omental fat not only makes the operation easier, but the chances of recurrence less.

OPERATIVE TECHNIC

As to the operation itself, an elliptic incision is made surrounding the old operative scar. The skin and scar within this incision are then excised. Care must be exercised in excising this tissue to prevent injury to the contents of the sac, as the sac is often adherent to the old scar, and if it is inadvertently opened some adherent viscus may be injured. After excising the scar, if the sac has not already been located, it is carefully searched for, and is usually found covered by little connective tissue. It is usually more convenient to open the sac, and, with one finger on the inside as a guide, to free it from the subcutaneous tissue by blunt dissection with a piece of gauze. However, if the sac is large and protruding viscera are apt to prove troublesome, it is better to free the sac before opening it. The sac should be freed down to its neck, and then the fascia carefully cleaned for 2 inches (5 cm.) in each direction from the hernial orifice. The sac is disposed of in the usual manner, after carefully freeing any adherent viscera that it may contain. Adherent omentum should be ligated and excised with the sac. Adherent bowel is easily injured, and, if necessary, islands

of the sac may be left attached to adherent loops, after the method of Cullen.[10] After the sac is excised, the peritoneum is usually best closed by a running stitch. In diffuse massive hernias where the intestines are everywhere adherent to the sac, it is futile and dangerous to attempt removal of the sac. In such cases, after freeing the sac, it should simply be pushed in and the repair made by one of the methods described, just as if the sac had been removed.

There are several methods of repair from which the surgeon has to choose. The older methods are well known and will not be discussed here. They include dissecting out the layers and overlapping the edges of the muscle and fascia in cases in which these structures can be approximated. In cases in which the edges of the defect cannot be approximated, flaps of the sheath of the rectus have been reflected to close the defect, and free transplants of autogenous fascia lata have been used. When any of these methods are used, it is my opinion that catgut should not be used in the repair. In large hernias, the tissues are always under some tension, and not infrequently quite a collection of serum develops between the subcutaneous tissue and fascia. This is due to the extensive dissection necessary in freeing the sac (which often burrows widely between the subcutaneous tissue and fascia) and clearing the fascia for repair. Under these circumstances there is always a tendency for the catgut, which is softened by the body juices, to become untied during the stress and strain of postoperative coughing, straining, retching, etc. Postoperative hernias repaired with catgut have been known to break down within the first few days following operation.

Gallie and LeMesurier[1] have devised an operation for postoperative hernia which has been widely used in recent years with more measure of success than has been obtained by the older methods. After dealing with the sac in the usual manner, they close the defect by a running suture of autogenous fascia lata strips. Before making this suture, the muscle and fascia about the hernial orifice are not separated into layers, as such a separation seems to weaken the grip of the fascial suture on the aponeurotic structures. These authors state that in most instances a single running stitch is all that is necessary to cure the hernia. However, when the opening is large or the closure is made under much tension, another lace-work of reenforcement sutures is superimposed over the first suture line. In cases in which the opening in the abdominal wall is so large that the edges cannot be approximated, the edges are drawn together as far as it seems safe, and the open space that is left is completely filled with a mesh-work of fascial sutures. These sutures have to be close enough together to preclude the possibility of a hernia occurring between them.

For several years I have used Gallie's technic in operating for postoperative hernia, but have substituted alcohol-preserved ox fascia for Gallie's living sutures. In hernias so large that the defect cannot be completely closed by approximating the fascial edges, it is closed as far as possible with a running stitch of preserved ox fascia, and then a free sheet of preserved ox fascia is sutured into the remaining defect with a continuation of the same stitch (fig. 3). Following this, a reenforcement lace-work suture line of fascia strips is placed over the implant (fig. 4). This method has given excellent results in the few cases in which it has been used. The method was used experimentally in dogs before being applied to human beings, and found to work satisfactorily, even in the presence of infection. In two experimental cases there was a large subcutaneous collection of pus forming a cystlike cavity. Autopsy was performed on one dog

10. Cullen, T. S.: Method of Dealing with Intestinal Loops Densely Adherent to an Umbilical Hernia, J. A. M. A. **78**:564 (Feb. 25) 1922.

a month after operation and the other four months after operation. In both cases the implanted sheet of fascia was found intact and covered with granulation tissue. More data with regard to the resistance of fascia to infection have been published elsewhere.[8]

In obese persons there is always a tendency for serum to collect between the fat and the fascia during the first few days following operation. This is especially true following the operation for massive hernias, in which there has been an extensive dissection and in which a large number of fascia strips have been used in making the repair. Such a collection of serum delays healing and may prove troublesome. In cases in which fat has been undermined over a large area in dissecting out a sac burrowing subcutaneously, it is a good plan to remove enough excess skin and fat to insure a snug closure. The redundance of skin and subcutaneous fat causes dead spaces, which invite serum collections.

Fig. 3.—Repair of a large postoperative hernia. The edges of the defect have been closed as far as possible with a running stitch of preserved ox fascia lata. The remainder of the defect has been closed by suturing in a free graft of preserved ox fascia lata, a strip of the same material being used as a continuous suture. The reenforcement stitch has been started and left loose showing the details of the lock stitches (Gallie technic).

Also in these cases I have recently been draining the undermined area with cigaret drains from a stab wound in the flank, made at the most dependent portion of the undermined area. Drains placed in the operative wound do not accomplish the desired result, but drainage from the stab wound permits the escape of any serum that collects, and the drains may be removed within the first few days after operation. Avoidance of these collections of serum is important, as they almost always become secondarily infected, and this may lead to the formation of a sinus which may be months in closing. This is especially true if nonabsorbable sutures have been used in the repair. In my experience,

however, an ultimate cure is far more likely to be secured when these sutures are used. It is far better to have a cure with a sinus that persists for a few months leading down to a nonabsorbable suture, than to have a recurrence soon after operation following the use of catgut. This, of course, applies to massive hernias that are closed under considerable tension and that are difficult to cure no matter what procedure is used. I have had no trouble with persisting sinuses since I have been using the stab wound in the flank to drain off serum collections. Before this, when employing drainage in the operative wound, I had several cases in which there were sinuses which persisted for months, but which did not prevent an ultimate cure. These sinuses were probably due to the fact that linen was used in tying off the ends of the fascia strips. I think that linen or silk should always be used for this purpose, instead of catgut or kangaroo tendon, as one cannot be sure how long the latter materials will resist absorption.

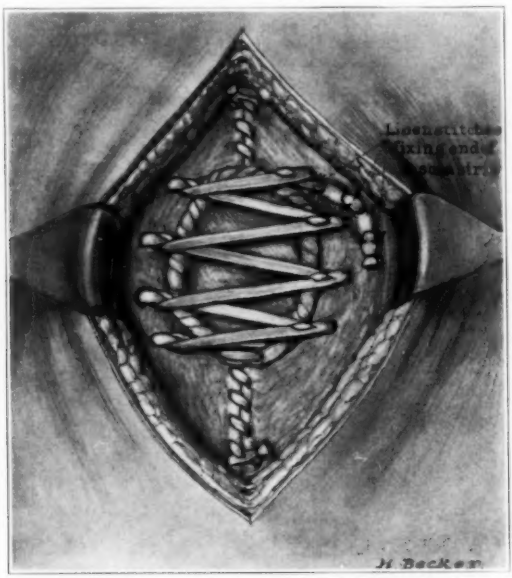

Fig. 4. — Repair of large postoperative hernia, showing the reenforcement lace-work of preserved ox fascia strips overlaying the free graft of the same material. The terminal end of the fascia strip is sutured in place with linen, instead of the end being split and tied into a knot as Gallie recommended.

It is important that the ends of the fascia strips remain tied off for a considerable length of time, as in most cases they are submitted to considerable stress. In one case I used no. 1 chromic catgut to tie off the ends of the fascia strips used in the repair of a massive postoperative hernia in an obese person. Following operation there was a large, subcutaneous collection of serum, and two days after operation the patient felt the wound give way in its deeper part. The skin did not break open, but the separated edges of the deep fascia could readily be palpated. It is safe to assume that the chromic catgut became softened by the collection of serum, and, being under considerable stress, some of the knots became untied and released the fascial ends, thus allowing the wounds to separate. Two years later this hernia, which was then even larger than at the time of the

first operation, was repaired in exactly the same manner, except that the ends of the fascia strips were tied with linen instead of catgut. Again there was a huge collection of serum, which drained for more than a week through a stab wound in the flank. Postoperative pneumonia also developed, and the patient coughed a great deal. In spite of all this, there has been no recurrence, although the second operation was done six months ago.

The prospect of cure in these cases depends on the size of the hernia, its location and the strength of the structures surrounding the defect. A hernia just under the costal margin is difficult to repair because of the rigidity of adjacent structures. A hernia appearing just above the pubic bones comes in the same category. I once repaired a massive hernia in this region by means of preserved fascia strips, but when the operation was over I was not satisfied that the defect was firmly closed at the lower border, which was formed by the unyielding pubic bone. A small recurrence soon appeared at this point. I am convinced that the proper procedure in this case would have been to drill holes in the pubic bone and to insure a cure by running the fascia strips through the holes in order to bring the abdominal fascia into snug apposition with the bone, thus effecting a secure closure of the lower border of the defect. An attempt had been made to run the fascia strips under the periosteum of the bone, but apparently the bite was not strong enough to be effective.

CONCLUSIONS

No one can see many large postoperative hernias and note the distressing symptoms and disabling effects that they produce without being impressed with the responsibility of the physician in seeking to avoid this almost entirely preventable condition. Small postoperative hernias are easy to cure, and large ones may be difficult or impossible to cure. This should always be carefully pointed out to the patient, and the natural tendency to put off the operation should be firmly discouraged.

STAB WOUND OF THE HEART

A REPORT OF TWO CASES

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It is with some hesitancy that I report these two cases of stab wound of the heart, with recovery in one after a cardiorrhaphy, as I realize that the operation of suturing the heart muscle in wounds of that organ has been performed many times during the last thirty years, with recovery of the patient in from 50 to 60 per cent of the cases, and that, in the last few years, much valuable work on the surgical treatment of the heart has been published. However, it must be recognized that all has not been learned concerning this condition, for the chance of seeing such cases does not come to every surgeon, and few see more than one, and as each case may present some particular condition not found in the others, there is reason for publishing its history so that a large number of cases may be collected for study. Unfortunately, most of the reported cases are the successful ones, while those in which the patients died are forgotten, though in many instances the findings, if reported, might have been of the greatest value, and a more exact rate of mortality would have been obtained. Therefore I am reporting two cases that contain facts of interest.

My first experience with a patient suffering from a wound of the heart occurred in 1915, at which time I operated on a man with a penetrating wound of the chest which involved the heart.

REPORT OF CASES

CASE 1.—*History.*—A man, aged 28, an Italian, was admitted to the prison ward at Bellevue Hospital on the morning of Sept. 22, 1915, having shortly before admission been stabbed in the chest with a large carving knife.

Examination.—The man was in an extreme state of shock and unconsciousness; respirations were rapid and labored. Over the edge and parallel to the left costal margin was an incised wound measuring about 1½ inches (3.5 cm.) in length, the mesial end of which was about ½ inch (1.3 cm.) from the midline. With every inspiratory movement of the chest there was a gush of dark blood from the wound.

Operation.—Since the operating room was prepared, the patient was immediately taken there, and, without anesthesia, a skin incision was made just lateral to the left border of the sternum at the level of the second costal cartilage and carried down to the fourth cartilage and thence obliquely outward. The skin flap so

formed was raised. The fourth and fifth costal cartilages were resected and the sixth and seventh divided. On entering the anterior mediastinum, a large amount of blood was evacuated and a wound was found which penetrated the wall of the chest immediately above the attachment of the diaphragm to the costal border. This was "sucking," and was found to communicate with the left pleural cavity, and to lead also into the pericardial sac. When the pericardium was opened, a large number of blood clots were found, and a wound 1 inch (2.5 cm.) in length was discovered on the anterior surface of the heart, along its lower border. From this a large quantity of blood spurted with each movement of the heart. An attempt was made to suture the wound, the heart being steadied by means of Allis clamps. However, before the suture was completed, the patient died. The estimated period of time from the infliction of the wound to the time of death was between three quarters of an hour and one hour.

Autopsy.—Autopsy was performed on September 22 by Dr. Otto Schultze, medical assistant to the District Attorney of New York County. The important facts discovered by this examination follow: The body was that of a young man, 5 feet 2¼ inches (158.1 cm.) in height, weighing 130 pounds (59 Kg.), with good muscular development. Rigor mortis was extremely marked. The mucous membranes of the lips were pale. The stab wound was found to be 1½ inches in length, situated on the left side of the anterior surface of the thorax, the upper end of the wound being ⅜ inch (1.2 cm.) to the left of the median line and the lower end ¾ inch (1.9 cm.) to the left of the median line, therefore being slightly oblique and situated over the cartilaginous margin of the thoracic wall. The wound passed through the seventh and eighth costal cartilages above the diaphragm and then through the pericardium, and also opened the left pleural cavity. The wound through the anterior wall of the pericardial sac extended from the diaphragm upward, and corresponded to the external wound, measuring 1¾ inches in length. The sutured wound of the ventricle was 1 inch in length and extended over the anterior surface of the right ventricle to the margin of the right ventricle at the junction with its diaphragmatic surface, corresponding in situation exactly with the stab wound described in the skin. There were two sutured wounds on the external surface of the left ventricle; one extended from the apex upward for a distance of ½ inch, the other wound was ¾ inch above and was identified as being produced by a clamp used to raise the heart at the time of operation. When the heart was opened, a wound through the interventricular septum was found, which measured 1 inch in length and corresponded in position with the external wound in the skin and with the wound in the wall of the right ventricle of the heart. The sutured wounds described on the external surface of the left ventricle showed no corresponding wound in the endocardium, so the knife passed through the wall of the right ventricle and interventricular septum. The thickness of the thoracic wall, including the costal cartilage, muscles and skin, was about 1 inch. The distance from the wound in the interventricular septum to the wound in the wall of the right ventricle was 2½ inches, allowing 1 inch for the thickness of the wall of the chest, so that the whole depth of the wound, from the skin to the interventricular septum, was 3½ inches.

The left lung was partly collapsed. Its pleural sac contained about 1 quart of bloody fluid and a few drachms of blood clot. The right pleural sac was obliterated by old adhesions.

All the organs showed signs of acute anemia.

Comment.—In case 1 it should be realized from the observations at autopsy that the extent of the injury was not of a type in which a

successful outcome could be expected, and it seems difficult to explain how the patient lived as long as he did, as death was apparently due to acute hemorrhage, cardiac tamponade playing little if any part in the fatal outcome. A break in the operative technic was made by grasping the surface of the heart with Allis clamps, as these tore the musculature.

However, the experience gained in this case stimulated further study in the hope that at some future date a similar injury might be seen. In the spring of 1927, the occasion arose.

CASE 2.—*History.*—A Negro, aged 23, was admitted to Lincoln Hospital at 11 a. m. on June 2, 1927, having just been stabbed in the chest with a pair of scissors.

Examination.—The patient was in deep shock, and it was difficult to arouse him; his skin was cold and clammy, his pulse was imperceptible at the wrist, and his heart sounds could not be heard. At a point level with and 1 inch to the right of the left nipple there was an incised wound measuring ¾ inch in length. The cardiac dulness was said to be enlarged to the left and downward. The pericardial sac was aspirated, and about 100 cc. of blood withdrawn; immediately following the aspiration, the patient's condition improved, and he apparently was more comfortable. At this time his temperature was 100 F., the pulse rate, 94 and the respiratory rate, 30. A roentgenogram, obtained with a portable apparatus, showed a general clouding of the lower left side of the chest.

I first saw the patient at 3 p. m., four hours following the injury. At this time the pulse was rapid but of fair quality. The apex beat was seen in the fifth interspace and the nipple line; the cardiac dulness apparently was not enlarged, and the heart sounds were normal. The blood pressure was 110 systolic and 76 diastolic. At 7:45 p. m., approximately nine hours after the injury, the patient's pulse became rapid and weak and the respirations dyspneic. The apex beat had disappeared, and the cardiac dulness was found to be enlarged to the left. The heart sounds were distant. The patient was operated on at 8:15 p. m., ten hours following the injury. Ether anesthesia was used.

Operation.—A vertical incision was made over the midline of the sternum at the level of the second rib and carried down to the level of the costal cartilage of the fifth rib. A second incision, starting at the latter point, was made for 3 inches (7.6 cm.) over the fifth costal cartilage and rib. The triangular flap thus formed was raised from the ribs and intercostal muscles. The perichondrium over the fourth and fifth ribs was separated, and the cartilages of the ribs were divided close to the sternum. The cartilages were then broken at their junction to the ribs. As soon as the cartilages of the fifth rib were separated from the underlying tissues, there was a gush of bright red blood, which was found to be emerging from a wound about 1 inch in length in the pericardial sac. The internal mammary artery was doubly ligated and divided. The third costal cartilage was separated at its junction with the sternum, and retracted upward and outward. The fibers of the triangular muscles were separated, and the pericardial sac exposed. The latter was opened by a vertical incision along the left border of the sternum for about 3 inches. In addition to the bright red blood that had already been evacuated, a large number of red and "chicken fat" clots were found in the pericardial sac. Two transverse wounds on the anterior surface of the left ventricle were found. A stay suture was placed in the apex of the heart, which steadied it enough to allow these incisions, which were bleeding, to be closed; the upper one with three interrupted sutures of no. 0 chromic catgut, the lower one by two interrupted sutures of the same material. The pericardium was closed by interrupted sutures of

chromic catgut, leaving about ¾ inch of the lower portion of the incision open, to which, but not through which, a rubber dam drain was connected. The muscles of the wall of the chest were closed with mattress sutures of chromic catgut, and the skin with interrupted silkworm-gut suture. The patient's condition was decidedly improved following operation.

The operation lasted for thirty-five minutes, and as soon as the intrapericardial tension was relieved the pulse became slower and of better quality. The pleural cavity was not opened either by the injury or by the operation.

Course.—The following morning the patient's condition was slightly improved, though he was still in a precarious condition. The pulse was of fair quality, regular and rapid; the temperature was 102 F., and he was still suffering a great deal from dyspnea, the respiratory rate being as high as 40. There was no cough. The dressings were slightly stained with blood. Examination of the blood showed: red blood cells, 3,900,000; hemoglobin, 78 per cent; white blood cells, 6,400; polymorphonuclears, 88 per cent, and monocytes, 12 per cent.

Suddenly that afternoon the patient's condition became worse, with signs of collapse, delirium, cold extremities, a pulse rate of 120 and labored respiration, 60 per minute.

The second day following operation, his condition was about the same: temperature, 103 F.; pulse rate, 120; respiration, 60, and a blood pressure of 130 systolic and 65 diastolic. The wound was dressed and the drain removed. The precordium was pulsating violently. A note made by the medical consultant was as follows: "At the outer border of the heart, there is a friction rub synchronous with respirations and with the heart beat, pleuropericardial. There are dulness over the base of the left lung, bronchial voice and breathing, consolidation and pneumonia in the lower lobe of the left lung."

The third day following the injury, the patient's condition continued the same, with labored respiration. A cough produced thick, yellowish sputum, streaked with blood. That afternoon the respiratory rate reached 70 per minute.

On the fourth day there was well marked dulness at the bases of both lungs, with crepitant râles. The sputum was decidedly rusty. On the ninth day, in his delirium, the patient jumped out of bed and ran the length of the ward. A roentgenogram of the chest on this day showed clouding of the entire right side of the chest, with the exception of small areas at the base and upper lobe of the lung. On the tenth day following admission, the patient's condition was decidedly improved. There were well marked signs over the right side of the chest of a hydropneumothorax, and aspiration produced thick, foul-smelling pus of a chocolate color, together with gas.

On June 15, thirteen days following the injury, the eighth right rib in the posterior axillary line was resected, and the right side of the chest drained. At this time an opening of an abscess on the surface of the lower lobe of the right lung was demonstrated. From that time the patient continued to improve; the temperature dropped gradually, but the respiratory rate stayed above 50 for at least two weeks longer. He was discharged from the hospital, with wounds healed, on July 22, forty-nine days after admission. He was seen two months after discharge, and he had returned to work and was apparently well. Unfortunately, he then disappeared from observation and could not be traced.

COMMENT

Case 2 presents a series of events that are of interest: a stab wound of the heart, which was probably only penetrating, followed by cardiac

tamponade, which was temporarily relieved by aspiration of the pericardial sac, and recurrence of the tamponade followed by pericardotomy and suture of the wounds in the musculature. A stormy convalescence ensued, pneumonitis of both lungs developing and an abscess of the right lung which ruptured into the pleural cavity, producing pyopneumothorax on the right side. The relation of the pneumonia to the injury of the heart is obscure. A roentgenogram of the chest, obtained some hours after the patient received the injury, though a poor film, showed general clouding of the entire left side of the chest. This was not due to hemothorax, as the pleural cavities were not opened at any time. The possibility of a coincident pneumonia has to be considered. The postoperative course of this patient was quite similar to that of a patient whose case was reported by Cole,[1] in whom there were definite physical signs of pneumonia the day following the injury. Recently Cox[2] reported a case that was followed by bronchial pneumonia in the left lung and fluid in both pleural cavities.

In comparing the two cases reported in this paper, it is evident that the type of injury in the first was severe and was not such that the patient could be benefited by operation. The wound in the wall of the chest was large and opened the left pleural cavity. The wound in the wall of the heart was long, perforating and in the vertical axis of the heart. It was situated in the right ventricle, and there was a second long wound in the intraventricular septum. There must have been a decided derangement of the circulation within the heart from the latter opening. There was free bleeding from the wound in the wall of the right ventricle, but no tamponade, as the blood passed directly from the pericardial sac into the left pleural cavity, from whence much escaped through the large wound in the wall of the chest on every respiratory movement. This patient apparently died from loss of blood and intracardial derangement of the circulation.

In case 2, the wound in the wall of the chest was small and did not enter the pleural cavity. Likewise, the opening in the pericardium was small. Though the wounds in the heart were small and nonperforating, they allowed sufficient blood to escape to produce increased intrapericardial pressure and cardiac tamponade. The cardiac tamponade was temporarily relieved by lowering of the intrapericardial pressure by means of aspiration, and it appeared for a time that further surgical intervention might not be needed, for the signs of cardiac tamponade did not reappear until a lapse of from seven to eight hours. Consequently, either the bleeding from the cardiac wound during this period

1. Cole, W. H.: Ann. Surg. **85**:647 (May) 1927.

2. Cox, D. M.: Wounds of the Heart; Report of Two Cases, Arch. Surg. **17**: 484 (Sept.) 1928.

must have been slight, though at operation a fair quantity of blood was found to be escaping from the wound in the wall of the heart, or a clot may have formed which prevented the bleeding for the time being, later becoming dislodged.

Wounds of the heart may be divided into those that only penetrate the musculature and those that perforate and enter one of the chambers. It is evident that the greatest number of cases that reach the surgeon are of the former type.

Perforated wounds are of necessity rapidly fatal, an example being case 1 reported in this paper. Wounds that penetrate the musculature but do not enter one of the chambers of the heart are not as rapidly fatal (case 2), unless a large branch of one of the coronary vessels is involved, for death in these cases is not due to the loss of blood but to the development of a cardiac tamponade, which, though bleeding slowly, may kill in a short period of time, as the pericardial sac is small and the membrane is nonexpansive. The position of the wound in most cases that reach the surgeon is found to be in the left ventricle, as its wall is the thickest, and consequently there is more chance that the wound is merely penetrating in character.

There is little doubt that every person with a wound of the heart should be operated on. This becomes imperative if he shows any signs of approaching cardiac tamponade. However, the aspiration of blood from the pericardial sac may be a life-saving procedure to reduce intrapericardial pressure temporarily in those cases in which the patient has not been seen until a marked degree of cardiac tamponade has developed, so that time may be obtained to make such preparations as are necessary for surgical intervention.

SUMMARY

Two cases of stab wounds of the chest that involved the heart are reported. In the first there was a perforating wound of the right ventricle which was rapidly fatal as a result of loss of blood. In the second there was a penetrating wound of the musculature of the left ventricle, a cardiac tamponade developing which was temporarily relieved by the aspiration of blood from the pericardial sac; this case later came to operation, and the wound was sutured. The patient recovered, following a stormy convalescence in which pneumonia of both lungs, an abscess of the right lung and empyema developed.

EXPOSURE OF THE HEART TO ATMOSPHERIC PRESSURE

EFFECTS ON THE CARDIAC OUTPUT AND BLOOD PRESSURE

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During the early part of the present century a great deal of attention was focused on the use of a chamber in which negative pressure could be maintained during operations on the chest. Such a chamber was devised by Sauerbruch [1] and was employed extensively in Germany. Subsequently this method was discarded because of the inconveniences which were associated with its use and because a method for inflating the lungs by positive pressure was devised. Recently Beck and his associates in this country have revived interest in the negative pressure chamber as a result of the experimental work that they have performed.

Beck and Cox [2] and Beck and Isaac [3] found that exposure of the heart of the dog to atmospheric pressure caused a rise in the venous pressure, a temporary decline in the arterial pressure and a decrease in the output of the heart. In the experiments of Beck and Cox [2] the output of the heart decreased from 15 to 30 per cent following the opening of the pericardium. Pneumothorax resulted in several of the dogs from the puncture holes in the pericardium. A few of the observations were made on unanesthetized dogs. Ether, amytal, ethyl carbamate or morphine was used as an anesthetic in most of the experiments. The later studies of Beck and Isaac [3] were performed on dogs that were profoundly anesthetized by morphine and sodium barbital. On opening the pericardial cavity to atmospheric pressure, a reduction in the output of the heart equal to 36 per cent of that obtained during the control period occurred. Negative pressure was then applied to the pericardial cavity. This resulted in a reduction of the venous pressure to approximately that obtained in the control period, but the cardiac output did not return nearly to the original level. The increase in the output of the heart was only 14 per cent.

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1. Sauerbruch, F.: Ueber die physiologischen und physikalischen Grundlagen bei intrathorakalen Eingriffen in meiner pneumatischen Operationskammer, Verhandl. d. deutsch. Gesellsch. f. Chir. **33**:103, 1904.

2. Beck, C. S., and Cox, W. V.: The Effect of Pericardiostomy on the Mechanics of the Circulation, Arch. Surg. **21**:1023 (Dec.) 1930.

3. Beck, C. S., and Isaac, Leabelle: Pneumocardiac Tamponade: A Study of the Effects of Atmospheric Pressure, Negative Pressure and Positive Pressure Upon the Heart, J. Thoracic Surg. **1**:124, 1931.

If the pressure of the atmosphere were responsible for the decrease in the output of the heart in the experiments referred to, it would appear that the application of negative pressure to the pericardial cavity should result in a return of the cardiac output to the previous level. In an effort to obtain further information on this point, it was decided to repeat some of the experiments of Beck and Isaac under slightly different conditions.

METHOD

Dogs were used in all experiments. Under ether anesthesia the pericardium was sutured to the wall of the chest by the method of Beck and Cox.[2] Following the healing of the incision and after varying intervals of time, the experimental determinations were performed. At least one hour prior to the control studies, the animals were given subcutaneously 0.065 Gm. of morphine. Using local anesthesia, a cannula that was connected to a mercury manometer was placed in the femoral artery for the determination of the arterial blood pressure. Maximum and minimum valves were used. The output of the heart was determined by the Fick principle, which is as follows:

$$\frac{\text{Cubic centimeters of oxygen consumed per minute}}{\text{Amt. oxygen taken up by 1 cc. blood in passing through lungs}} = \text{Cardiac output per min.}$$

The consumption of oxygen was determined by the use of a Benedict spirometer. The arterial sample of blood was obtained from the femoral artery, and the mixed venous sample was obtained by puncture of the right side of the heart. The latter puncture was made through the wall of the chest in getting the blood for the control determinations. Thereafter it was made through the pericardiostomy opening. In some experiments the blood that was removed was replaced by an equal amount. The oxygen content of the blood was determined on the Van Slyke-Neill manometric apparatus.

After the completion of the control determinations, the site of the previous operation was infiltrated with procaine hydrochloride, and an opening 2 cm. square was made in the pericardium. Studies were performed thirty minutes after the pericardium was opened and at varying intervals thereafter. At the completion of the experiments, the animals were killed and autopsy was performed.

RESULTS

In the first two experiments the pericardium was opened two weeks after it had been sutured to the wall of the chest. This procedure was believed to be associated with the production of a pneumothorax. The output of the heart decreased, and the arterial blood pressure declined slightly. It was decided that it was necessary to allow a longer interval of time to elapse between the original operation of suturing the pericardium to the wall of the chest and the pericardiostomy if pneumothorax was to be avoided. The results of an experiment in which it was thought that the incision was accompanied by the entrance of air into the pleural cavity are given in table 1. There was a slight decline in the output of the heart shortly following the incision, which later

TABLE 1.—*The Effects of Pericardiostomy on the Cardiac Output and Blood Pressure* *

Time	Weight, Kg.	Arterial Oxygen, per Cent by Vol.	Venous Oxygen, per Cent by Vol.	Arteriovenous Difference, per Cent by Vol.	Maximum Blood Pressure, Mm. Hg	Minimum Blood Pressure, Mm. Hg	Consumption of Oxygen, Cc. per Min.	Cardiac Output per Min., Cc.
Control	12.0	18.84	13.28	5.56	163	85	92.43	1,662
30 minutes after pericardiostomy	....	20.22	13.68	6.54	163	79	90.41	1,383
1¾ hours after pericardiostomy	....	19.80	15.24	4.56	163	79	83.95	1,841

* Jan. 12, 1932: The pericardium was sutured to the wall of the chest.
Jan. 28: Determinations were made. On opening the pericardium a sucking sound was audible. It was feared that the dog got a small amount of air in the pleural cavity.

TABLE 2.—*The Effects of Pericardiostomy on the Cardiac Output and Blood Pressure* *

Time	Weight, Kg.	Arterial Oxygen, per Cent by Vol.	Venous Oxygen, per Cent by Vol.	Arteriovenous Difference, per Cent by Vol.	Maximum Blood Pressure, Mm. Hg	Minimum Blood Pressure, Mm. Hg	Consumption of Oxygen, Cc. per Min.	Cardiac Output per Min., Cc.
Control	10.0	14.28	7.20	7.08	156	58	78.8	1,113
30 minutes after opening pericardium	....	15.22	8.88	6.34	152	60	97.8	1,543
95 minutes after opening pericardium	....	15.72	8.86	6.86	124	78	93.2	1,359

* Feb. 11, 1932: The pericardium was sutured to the wall of the chest.
March 9: Studies were performed. The pericardium was securely anchored to the wall of the chest in the neighborhood of the incision. No pneumothorax resulted.

TABLE 3.—*The Effects of Pericardiostomy on the Cardiac Output and Blood Pressure* *

Time	Weight, Kg.	Arterial Oxygen, per Cent by Vol.	Venous Oxygen, per Cent by Vol.	Arteriovenous Difference, per Cent by Vol.	Maximum Blood Pressure, Mm. Hg	Minimum Blood Pressure, Mm. Hg	Consumption of Oxygen, Cc. per Min.	Cardiac Output per Min., Cc.
Control	14.0	18.48	12.90	5.58	182	96	65.3	1,170
30 minutes after operation	....	19.08	15.00	4.08	176	86	80.3	1,968
2½ hours after operation	....	18.96	12.80	6.16	193	99	90.4	1,468

* Feb. 10, 1932: The pericardium was sutured to the wall of the chest.
March 11: Studies were performed. At autopsy the pericardium was found to be securely anchored to the wall of the chest. There was no thickening of the mediastinal pleura or collapse of the lungs.

TABLE 4.—*The Effects of Pericardiostomy on the Cardiac Output and Blood Pressure* *

Time	Weight, Kg.	Arterial Oxygen, per Cent by Vol.	Venous Oxygen, per Cent by Vol.	Arteriovenous Difference, per Cent by Vol.	Maximum Blood Pressure, Mm. Hg	Minimum Blood Pressure, Mm. Hg	Consumption of Oxygen, Cc. per Min.	Cardiac Output per Min., Cc.
Control	18.0	19.08	13.02	6.06	175	84	108.3	1,787
30 minutes after operation	....	18.36	12.86	5.50	172	85	122.0	2,218
3¼ hours after operation	....	20.04	11.82	8.22	190	104	142.1	1,729

* Dec. 31, 1931: The pericardium was sutured to the wall of the chest.
March 21, 1932: Studies were performed. At autopsy the pericardium was found to be securely anchored at all points adjacent to the incision.

TABLE 5.—*The Effects of Pericardiostomy on the Cardiac Output and Blood Pressure* *

Time	Weight, Kg.	Arterial Oxygen, per Cent by Vol.	Venous Oxygen, per Cent by Vol.	Arteriovenous Difference, per Cent by Vol.	Maximum Blood Pressure, Mm. Hg	Minimum Blood Pressure, Mm. Hg	Consumption of Oxygen, Cc. per Min.	Cardiac Output per Min., Cc.
Control	14.2	14.34	10.72	3.62	187	77	89.3	2,467
30 minutes after opening pericardium	....	15.42	10.30	5.12	176	73	116.2	2,270
2½ hours after operation	....	14.10	9.66	4.44	166	86	96.3	2,171
4½ hours after operation	....	14.02	9.36	4.66	165	87	94.1	2,019

* Jan. 12, 1932: The pericardium was sutured to the wall of the chest.
March 22: Studies were performed. No opening into the pleural cavity was found at autopsy. Immediately after opening the pericardium a sucking sound was heard, which was believed not to be due to an opening into the pleural cavity but to air entering and leaving the pericardial cavity.

TABLE 6.—*The Effects of Pericardiostomy on the Cardiac Output and Blood Pressure* *

Time	Weight, Kg.	Arterial Oxygen, per Cent by Vol.	Venous Oxygen, per Cent by Vol.	Arteriovenous Difference, per Cent by Vol.	Maximum Blood Pressure, Mm. Hg	Minimum Blood Pressure, Mm. Hg	Consumption of Oxygen, Cc. per Min.	Cardiac Output per Min., Cc.
Control	16.1	23.16	18.72	4.44	186	95	177.1	3,989
30 minutes after pericardiostomy	....	22.92	18.00	4.92	188	95	179.3	3,644

* March 23, 1932: The pericardium was sutured to the wall of the chest.
May 6: Studies were performed. No pneumothorax resulted.

returned to a level that was slightly higher than that existing before. The arterial blood pressure was unaltered. In the remaining experiments from four to ten weeks separated the original operation and the subsequent studies.

In one experiment the animal was not quieted by morphine, and sodium barbital was injected intravenously. A rather marked decrease in the output of the heart was noted following the pericardiostomy. The findings in this experiment are in accord with those of Beck and Isaac.[3]

In the remaining five experiments morphine, supplemented by the local injection of procaine hydrochloride, was used as the anesthetic. The output of the heart in three of the five experiments was found to be greater following the opening of the pericardium than it had been previously, while in two of the experiments it was somewhat lower. In most of the experiments the alterations were probably within the limits of error of the method and of the normal variations in the output of the heart. The maximum and minimum arterial blood pressures remained remarkably constant except for a decline in the maximum pressure and a rise in the minimum pressure shortly before the completion of one of the experiments. The results of these experiments are given in tables 2, 3, 4, 5 and 6.

COMMENT

If a method were available by which the output of the heart could be determined immediately after exposure of the heart to the pressure of the atmosphere, quite likely a decrease in the output would be found. This pressure on the veins at the base of the heart is probably associated with an initial decrease in the amount of blood returning to the heart and hence with a decrease in the cardiac output. The studies reported here indicate that this decrease, if present, is only temporary. If marked disease of the circulatory system were present, it is doubtful if this readjustment would take place. Evidence on this point is lacking, as the present experiments and those of Beck and his associates were performed on normal dogs.

There are several objections to the use of a chamber in which the pressure is maintained at a constant negative level. The negative pressure in the pleural and pericardial cavities is constantly changing, and a large part of its beneficial effect is due to this characteristic. In the chamber that was devised by Sauerbruch the negative pressure was applied to every part of the patient's body surface except for the head and part of the neck. Certainly some of the desirable effects of having a negative pressure at the site of the veins entering the pericardium will be counterbalanced by also having a negative pressure existing around the abdomen and extremities. It is the difference between the pressures existing in the chest cavity and those in the rest

of the body that is important in influencing the return of blood to the heart. It has recently been found by Harrison [4] that the alternate application of positive and negative pressures to all of the body except the head, sufficient to produce overventilation, is associated with a decrease in the cardiac output. The full advantages of the negative pressure chamber would be realized if it included only the chest and if the pressure fluctuated.

SUMMARY

The cardiac output and the maximum and minimum arterial blood pressures of dogs were determined before and after the exposure of the heart to atmospheric pressure. No definite alterations in the arterial pressures were noted, and the changes in the output of the heart were not marked. In some experiments the cardiac output increased slightly, and in others it decreased slightly. Indications for the use of the Sauerbruch negative pressure chamber are not supplied by the results of these experiments on normal dogs. Some of the undesirable features of the apparatus are described.

4. Harrison, T. R.: Personal communication to the author (1932).

A REVIEW OF UROLOGIC SURGERY

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KIDNEY

Anomalies.—Friberg [1] reported a case of double kidney in which there were hydronephrosis and a stone in one of the renal pelves. The diagnosis was made before operation. Heminephrectomy was performed, after which the patient recovered.

Rumpel [2] described a case of a one-sided "Langniere," so-called crossed dystrophy, in which the entire fused renal mass was on one side. The lower kidney was pyonephrotic. A median line abdominal incision was made; the destroyed renal segment was resected and removed transperitoneally.

Pierson [3] stated that true unilateral fusion of the kidneys is one of the rarest types of renal anomaly. Morris found only 1 case in 15,908 postmortem examinations, and Steward and Lodge reported 1 in 6,500. In some cases the condition has been observed at birth and in the eighth decade, but it occurs most frequently in the third decade.

The symptoms of this anomaly arise from its complications. Pain is the most common symptom, and may vary from only slight discom-

1. Friberg, Sten: Heminephrektomie bei einer Niere mit zwei Ureteren mit Hydronephrose und Stein im einen Nierenbecken, Acta chir. Scandinav. **69**:393 (March 3) 1932.

2. Rumpel, O.: Nierenresektion bei einseitiger Langniere (gekreuzte Dystopie), Zentralbl. f. Chir. **59**:1290 (May 21) 1932.

3. Pierson, L. E.: Unilateral Fused Kidney, J. Urol. **28**:217 (Aug.) 1932.

fort in the back or abdomen to severe pain, which may resemble that of a calculus, as was demonstrated in Pierson's case. All types of anomalies in fusion are potential factors in the production of dystocia. Because of the fact that true unilateral fused kidneys lie higher in the abdomen than anomalies of the pelvis, there is less tendency for such a complication.

The treatment of this condition, as in the case of any renal anomaly, depends on the complications, such as infection, calculus or other pathologic conditions. In these cases the complication alone is treated. Pierson reported 1 case of unilateral fused kidney, making a total of 103 cases reported in the literature.

[COMPILERS' NOTE.—The clinical symptoms observed in anomalies of the upper part of the urinary tract are important because they may mislead in the diagnosis and, without any evidence of complications or associated pathologic changes, the patients may have severe pain in the back or in the abdomen. The pain may be directly due to pressure exerted by the anomalous organ on surrounding anatomic structures. A urographic examination should be made if the condition is suggestive of a renal anomaly, in an effort to ascertain whether this is present. The treatment should not always be directed entirely to the associated changes, but also to the anomaly itself. In cases of horseshoe kidney, a division of the isthmus and nephropexy at times relieve the clinical symptoms and prevent the occurrence of further changes by securing a better position and better drainage for the organ.]

Stone.—Papin [4] analyzed 136 cases of renal lithiasis. The indications for radical and conservative operation were considered, as well as what he considered the best conservative procedures.

Sixty-five of the 136 patients had had nephrectomy performed, 64 had conservative operations, and for 7 all types of surgical intervention were contraindicated. Successful results were obtained in 56 cases following nephrectomy. Five of the remaining 9 patients died of operative shock resulting from the removal of large infected kidneys; the other 4 patients died of pulmonary congestion, rupture of an abnormal artery and fistula of the small intestine. Nephrectomy was indicated for the following conditions: hydronephrosis, 17 cases; calculous pyonephrosis, 11; coralliform stones, 16; large stones, 6, and multiple stones, 6; pyelotomy was impossible and nephrotomy dangerous in 2. There was 1 case each of atrophic kidney, retrorenal abscess with an infected kidney, pelvic kidney, horseshoe kidney with a fistula, a fistula persisting after nephrotomy, rupture of the ureter and rupture of an abnormal renal vein.

4. Papin, Edmond: Étude sur la chirurgie de la lithiase rénale et en particulier sur les méthodes conservatrices, Arch. d. mal. d. reins **6**:493 (May) 1932.

Four (6.25 per cent) of the 64 patients treated conservatively died; 3 of these deaths were in the series of 12 cases in which nephrectomy was performed, and 1 occurred following pyelotomy with suppuration of the kidney, which required secondary nephrectomy. This case represented 1.9 per cent of the 52 cases in which pyelotomy was performed. Hemorrhage occurred from the wound in 1 case, and there were repeated internal hemorrhages in another case eight and fifteen days after operation. Recurrence of stone on the same side was observed in 5 cases, three, five and six years following operation, and on the opposite side in 1 case ten years afterward. Bilateral calculi occurred in 3 cases. A conservative operation was made possible by a complete roentgenographic examination, with both ascending and descending pyelography, an incision of limited scope, improved methods of suture, drainage of the cavities of the kidney and of the renal fossa and replacement of the kidney by means of nephropexy over pledgets of adipose tissue.

Various types of incisions were used. In 10 cases pelvionephrolithotomy was performed with good results. In several cases the lower pole of the kidney was freely incised and the incision prolonged, when necessary, over the inferior margin of the large lower calyx. In other cases the parenchyma was incised along the oblique fold which forms a continuation of the posterior lip of the hilus. This was done sometimes before and sometimes after the pelvis was opened, and by two different methods: either by a free incision from outside inward, or by passing a blunt Reverdin needle between the posterior surface of the pelvis and the large lower calyx on the one hand and the wall of the sinus on the other, and then through the parenchyma, carrying a silkworm suture which was pulled through the parenchyma. Such an incision seldom bled, and catgut sutures over pledgets of fat gave satisfactory hemostasis. If the pyelonephrotomy was extensive, Papin always sutured the pelvis first, and then the parenchyma above it. In many cases of small stones without much infection the pelvis was left open and the renal area drained. In the majority of cases, transrenal drainage was established. Fixation of the kidney is important. Papin always replaced the kidney in a high position, suspending it hammock-fashion by means of its capsule. Whenever the kidney was movable, nephropexy was performed at the upper pole.

[COMPILERS' NOTE.—In general, the material reviewed by Papin brings out several features of renal lithiasis: 1. Early recognition of the disease is associated with a more conservative operative procedure, which may be undertaken with a slight risk. 2. In a variable number of cases (from 4 to 20 per cent), dependent on the chemical type of calculus and the nature of the infection, renal lithiasis is recurrent,

and prophylactic treatment against recurrence over a period of years must be carefully carried out. 3. The author's advocacy of surgical drainage of the kidney and its fixation in a position to insure adequate physiologic drainage is noteworthy, as these features constitute pertinent factors in restoring the kidney to an uninfected state and to a maximal degree of functional capacity. 4. The selection of cases for nephrectomy or for conservative operation will depend on the operator's surgical judgment in each case. Papin's estimate of good results following nephrectomy fairly well paralleled those in which conservative incisions on the kidney or renal pelvis were undertaken. His criteria for nephrectomy are well founded. Furthermore, they are consistent with the clinical judgment of most urologists, in spite of the present-day well merited emphasis that is being placed by American surgeons on conservative renal operations.]

Scholl [5] reported 2 cases of bacterial concretions in the renal pelvis. In both cases it was possible to obtain cultures of active colon bacilli or a positive culture from any part of the stones, either on the surface or from the cut section. In each case the kidney was either partially or almost totally destroyed and in such a condition that it would have been impossible to obtain permanent cure by attempting to remove the fragments of stone.

With regard to the etiology, it was thought that primarily there was some kind of nucleus, and secondarily that there was some type of cementing process which caused the masses of bacteria to adhere. There seems to be little doubt that the concretions develop by continual proliferation of live bacteria and the addition of cells to the exterior of the growing mass. It is also believed that the presence of necrotic shreds cast from the wall of the renal pelvis in pyelitis may form the nucleus. Many of the patients gave a history of old pyelitis. Some investigators are of the opinion that the first event is simple adhesions of bacteria that form small masses. The most significant factor in these cases seems to be the continuous deposit of bacteria in the renal pelvis.

Heitz-Boyer [6] stated that he has used roentgen rays for some time in operations on the kidney, and wished to extend the practice to operations on the lungs and to fractures. The roentgen rays are indispensable to locate small stones when operating and in cases of multiple calculi to ascertain that none has been overlooked. Some small round stones are known to move freely about in a dilated pelvis, and may even enter the ureter.

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5. Scholl, A. J.: Bacterial Concretions in the Kidney Pelvis with Report of Two Personal Cases, Surg., Gynec. & Obst. **55**:360 (Sept.) 1932.

6. Heitz-Boyer: Sur la lithiase rénale et sa technique opératoire, Bull. et mém. Soc. nat. de chir. **58**:216 (Feb. 13); 386 (March 12) 1932.

Heitz-Boyer expressed the belief that the roentgen ray apparatus should be equipped for taking roentgenograms as well as for fluoroscopic examination, and that it should permit examination at different angles.

Oehlecker [7] reported a case of stones in the kidney which developed after trauma. The patient, a man, aged 45, had suffered a number of fractures and was in bed for some time. A roentgenogram taken at the time of the injury showed no evidence of renal stones. Seven weeks later, symptoms of renal calculus developed. A roentgenogram at that time and at intervals thereafter indicated the definite development of calculi in both kidneys.

The author expressed the belief that the development of stones in this case was due to injury to the kidneys and formation of blood clots in the renal pelvis, which served as a nucleus. Kümmell and Graff have described this condition following renal injury and formation of blood clots. Another type of stone in the kidney develops after extensive injury and fracture of the vertebrae with paralysis of the bladder. In such cases the formation of stone is due to retention of urine in the bladder, causing urinary infection which ascends to the renal pelvis and in that manner forms a stone.

In Walters' [8] review of urologic surgery from the Mayo Clinic for 1931, 60 cases were cited in which stones were removed from the kidney. In many instances the stones were multiple, combined with mild degrees of pyelonephritis or hydronephrosis. In 6 cases plastic operations were performed on the renal pelvis for relief of associated hydronephrosis. Calculi were removed from the ureter by cystoscopic manipulation in 20 cases and by ureterolithotomy in 52. No deaths occurred among the 66 patients from whose kidneys stones were removed; 1 death occurred in the group from whose ureters stones were removed.

Nephrostomy was performed in 27 cases, and pelviostomy in 5, usually as an adjunct to plastic operations on the renal pelvis for hydropnephrosis and for multiple renal calculi associated with renal infection. Nephrectomy was performed in 135 cases. The larger groups included 34 cases in which nephrectomy was performed for removal of a unilateral tuberculous kidney. The kidney was removed in 26 cases because of nephrolithiasis, in 28 cases because of malignant tumors and in 27 cases because of marked unilateral hydronephrosis in which a conservative operation was not warranted. Two patients died fol-

7. Oehlecker, F.: Zur traumatischen Entstehung von Nierensteinen, Zentralbl. f. Chir. **59**:1264 (May 21) 1932.

8. Walters, Waltman: Report of Urologic Surgery (Exclusive of Gynecologic Surgery) for 1931, Proc. Staff Meet., Mayo Clin. **7**:245 (April 27) 1932.

lowing removal of a large adenocarcinoma of the kidney. Three operations were performed in cases of horseshoe kidney, heminephrectomy being done in 1 case, pelviolithotomy in the second and reimplantation of the ureter in the third for the relief of unilateral hydronephrosis. All these patients recovered.

Colic.—Nuvoli and Impiombato[9] reported 150 cases in which there was renal colic and in only 26 of which there was accompanying calculosis, as shown by roentgenograms. In 134 cases there were alterations in the vertebral column. Two types of regional anomaly were found: The twelfth thoracic and first lumbar vertebrae were of a transitional character, or there was sacralization of the fifth lumbar vertebra or lumbarization of the first sacral metamere. Numerical variations were also observed, such as a sacrum with 3, 4 or 6 metameres, and a lumbar spine with 4 or 6 vertebrae. In the cases of spina bifida the neural arch was generally either fissured or entirely wanting. Another type of variation was the prolongation downward, beyond the fourth sacral segment, of the terminal hiatus.

The pathogenesis of the spasms of the urinary passages was undoubtedly associated with these deformities. The majority of the patients had had painful symptoms in the right and then in the left lumbar region, or on one side only, over a period of years. These symptoms often culminated in attacks of colic with diminished urination, vesical tenesmus and terminal hematuria. Clinical study may give negative results or disclose painful points corresponding to the sites of the kidneys and ureters. Urologic examination often yields negative results. Since calculosis also occurs with congenital changes of the spinal column, it may be assumed that one of the pathogenic factors, namely, spasm, is common to both types of cases. In patients predisposed to the formation and elimination of large quantities of salts in general, the stasis produced by spastic contraction in all the urinary passages or at any single point in the tract favors deposition of the salts themselves in the form of calculi. The spastic contractions may last a long time and constitute an almost permanent obstacle to urinary outflow. The malformation of the spinal column seems to be responsible for special nerve changes which create dyskinesia of the urinary passages, leading to chronic stasis and culminating in acute spastic attacks which produce colic.

Either of two hypotheses may be assumed to explain the hematuria often present in these cases of noncalculous colic: The spasm creates acute upward distention, causing rupture of some thin vessel, or spastic contraction at the level of the calices, pelvis or ureter may be sufficient

9. Nuvoli, Umberto, and Impiombato, Gastone: Sindromi di calcolosi urinaria e malformazioni della colonna vertebrale, Arch. ital. d. urol. **7**:589 (July) 1931.

to close the venous vessels and cause engorgement from stasis, with extravasation of blood corpuscles.

Study of the development of the spinal nerves in relation to that of the vertebral column shows that the column evolves parallel to the nerves themselves at about the eighth week; hence every disturbance of the former may reflect on the development of the nerves and their roots. Morphologic changes of the spine at this period will be able to make themselves evident not only on the peripheral nervous system but on the sympathetic autonomic system and its innervations.

[COMPILERS' NOTE.—It is important that urologists, orthopedic surgeons and gynecologists cooperate to clarify the obscure syndromes of colic without calculi, backache, idiopathic hematuria and other urinary symptoms or without definite lesions in the genito-urinary and gynecologic tract. It is obvious that roentgenographic examination in many of these cases may be the means of diagnosis, but the fact must not be overlooked that the pelvis of the kidney is often misplaced and that sometimes the presence of cystine and uric acid stones in the upper part of the urinary tract is not detected by roentgen rays. Many cases have been reported in which the shadow of a stone in the renal pelvis is unusual and situated so close to the spinal column that it is overlooked, and the patient is mistakenly referred to the orthopedic surgeon or the neurosurgeon. A clear description has also been given in the literature, especially by Bransford Lewis, of regurgitation renal colic or the so-called vesicorenal reflux, in which, for lack of a sphincter in the mouth of the ureteral orifice, the vesical contents regurgitate into the kidney, causing sudden renal colic. These urologic problems are always of interest to the urologist, and can be accurately detected by urography.]

Hydronephrosis.—Ceccarelli [10] reported a series of experiments to determine changes that occur in a hydronephrotic kidney after ligation of one or both renal vessels. In experimenting with dogs it was observed that renal function continued for some time after ligation, so that if the ureter were tied also, hydronephrosis could be produced. At the same time sclerosis slowly supervened, invading the entire organ and resulting in vast zones of calcareous infiltration. Adult rabbits were then used for experimentation. After lumbotomy, the ureter was tied about 2 cm. from the pelvis. After from twenty to fifty days a second operation by the abdominal route was performed. It was proved that hydronephrosis had developed in almost every case; the vascular pedicle, or the artery alone in a few cases, was then tied. Laparotomy was chosen as the second type of operation because the right pedicle could be reached without destroying the vascular adhesions established

10. Ceccarelli, G.: Sulle modificazioni delle sacche idronefrotiche dopo legatura del peduncolo vasale, Arch. ital. d. urol. **7**:614 (July) 1931.

between the kidney and the surrounding tissue after lumbotomy. These were particularly important in this case, owing to their relation to the trophism of the organ, in view of the abundance of vessels which the capsule of the hydronephrotic sac possesses.

Necropsy was performed from thirty days to three months after the second operation. The results varied according to the length of time that the hydronephrotic state had existed. The rapid atrophy of the organ was accompanied by sclerosis with calcareous infiltration and osseous new growth. The growth is of a certain biologic interest, since it may possibly be deduced from this that it is independent of the presence of preexistent medullary germs in the kidney, as Sacerdotti and Frattini have contended.

Ceccarelli expressed the opinion that the osseous new growth in his experiments occurred earlier and more rapidly than in normal dogs in which the emulgents had been tied, and that this might bear some relation to the presence of the liquid contained in the pelvis, which was rich in salts of calcium. It was concluded that the ligation of the vascular pedicle of the kidney that had been rendered hydronephrotic caused rapid atrophy of the organ, which became transformed into a small nodule of connective tissue. In the rabbit, in addition to the zones of calcareous infiltration, a typical osseous new growth was produced, whereas the liquid of the sac was totally absorbed.

Moore [11] stated that unilateral renal agenesia occurs infrequently, but the status of the opposite kidney must be determined as a routine measure in any case in which nephrectomy is contemplated. In the conservative treatment of hydronephrosis the merits of the various methods for correcting obstructive conditions at the ureteropelvic juncture must be considered in their application to the individual case at the time of operation. The factor of renal counterbalance is important in unilateral hydronephrosis; experiments on animals have not revealed positive proof as to whether atrophy from disuse of the diseased kidney occurs after the other organ has undergone compensatory hypertrophy.

A case is reported in which was present a large infected hydronephrosis caused by a valvular type of obstruction, with congenital absence of the opposite kidney. The method of relieving the obstruction, together with the functional and urographic end-results, is presented.

Johnson [12] dissected and examined the renal tubules (after the method of Huber) in progressive hydronephrosis in order to determine

11. Moore, T. D.: Congenital Solitary Hydronephrotic Infected Kidney: Pyeloureteroplasty, J. Urol. **27**:581 (May) 1932.

12. Johnson, C. M.: The Pathogenesis of Hydronephrosis, J. Urol. **27**:279 (March) 1932.

what changes occur. Dilatation begins at the glomerulus, and proceeds quickly and evenly to the papillary ducts by the end of two or three weeks. By the end of one month there is beginning atrophy in the glomerulus and proximal convoluted tubules, with some dilatation still present in the distal convoluted and collecting tubules. From this point there are progressive atrophy of the glomeruli and convoluted tubules and progressive dilatation of the collecting tubules in the medulla. By the end of three months some glomeruli may be directly in communication with collecting tubules, owing to the shortening, straightening and disappearance of the convoluted tubules. Others never reach this stage, but undergo atrophy and lose their communication with the collecting tubules after four or five months. A maximal degree of dilatation of the remaining collecting tubules in the medulla is reached at five months. Gradual atrophy and shrinkage in all dimensions then take place.

Cysts.—Jeanneney [13] reported a case in which echinococcus cyst of the kidney was successfully treated by nephrectomy. Hydatid cysts of the kidney are rare and sometimes difficult to diagnose. Of 446 cases of echinococcus disease, Nicaise found that several cysts occurred in 1 kidney alone in 20 cases, that the cysts were bilateral in 12 cases and that the cysts in the kidney were associated with disease in organs such as the liver or the lungs in 58 cases.

The cyst is usually at the level of the superior pole, and at times it may open into the pelvis. It sometimes is well encapsulated and easy to remove. In other cases it is so adherent that part of the renal substance has to be removed with it. Various surgical procedures have been successfully performed, such as marsupialization (sewing of the edges of the cyst cavity to the margin of the incision), puncture of the cyst and drainage, total or partial enucleation and total or partial nephrectomy.

Neff [14] reported a case of massive hemorrhagic cyst in a Wilms tumor. The entire renal mass removed at operation weighed 11 pounds (5 Kg.) and measured 40 by 25 cm. Preliminary aspiration of the contained fluid was done before the removal of the mass. Five solitary cysts larger than the cyst reported by Neff were reviewed from the literature. Cassioli's specimen contained 12 liters; Lockyer's, 25 pints (12.5 liters); Lamson's, 11 to 12 quarts (11 to 12 liters); Krogius' 10 liters, and Archer's, 9 quarts (9 liters). Cassioli's cyst was marsupialized. Nephrectomy was done for the other 4 cysts.

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13. Jeanneney, G.: L'échinococcose rénale, Bordeaux chir. **3**:36 (Jan.) 1932.

14. Neff, J. H.: Massive Hemorrhagic Cyst in a Wilms Tumor of the Kidney in an Adult, J. Urol. **28**:65 (July) 1932.

Carbuncle.—Ljunggren [15] stated that carbuncle of the kidney probably occurs more commonly than is indicated by the 50 cases reported in the literature. The diagnosis of this lesion will unquestionably be made more often when symptoms are better known. Renal carbuncle usually results from a break in the fatty capsule with a perinephritic abscess. As a rule, there is a previous history of furuncle or carbuncle. The patient is generally acutely ill with high fever, which may be sustained or intermittent. Urinary symptoms appear only when pyelitis occurs. There is usually pain on the affected side, with tenderness on pressure over the affected area, as well as some spasticity of muscles. Eventual swelling in the flank does not exclude the possibility of carbuncle of the kidney; it generally suggests associated paranephritic abscess. Occasionally, there may be hematuria detectable only microscopically, a few pus cells, a trace of albumin and at times some staphylococci.

It is often difficult to distinguish carbuncle of the kidney from abscess of the kidney, purulent pyelonephritis and formation of pus in the renal hilus. The diagnosis often cannot be made until after an exploratory operation. As a rule, pyelography does not help in making a definite diagnosis, although a case was cited in which deformity caused by pressure of the lower calyx of the right kidney was noted. At nephrectomy the kidney was seen to contain a carbuncle in the lower pole. Although it was known that there was a staphylococcus infection, the pyelogram was the factor aiding in the determination of the differential diagnosis.

Trauma.—Bonhoff [16] reported a case of extensive subcutaneous cross-tear of the kidney, which resulted from a relatively slight injury. The patient struck his back on the edge of a stone wall. Bonhoff attributed the injury not so much to the actual trauma against the wall as to the secondary extensive contraction of the abdominal muscles, which caused a strong hydraulic pressure on the abdominal contents. The injury to the kidney was not a definite tear but, as the author described it, a rupture of the entire renal mass. Early surgical intervention is indicated in these cases, not only to aid in making an accurate diagnosis but to institute treatment before extensive bleeding causes complications. If the injury is extensive, Bonhoff's belief coincides with that of Kümmell, that nephrectomy is the quickest and safest method of treating the condition.

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15. Ljunggren, Einar: Beitrag zur Röntgendiagnostik der Nierenkarbunkel, Ztschr. f. urol. Chir. **31**:258, 1932.

16. Bonhoff, Friedrich: Schwere subkutane Nierenzerreibung durch relativ leichtes Trauma, mit Bemerkungen über den Verletzungsmechanismus, Zentralbl. f. Chir. **59**:1331 (May 21) 1932.

Rupture of Renal Artery.— Edmunds [17] reported a case of rupture of a left renal artery following trauma and without injury to the kidney. A man, aged 45, fell about 25 feet (7.6 meters). First aid was given; two hours later the patient was in extreme shock. An exploratory operation by means of a left rectus incision was performed. The spleen was found ruptured transversely. The upper pole lay free in the abdomen; the lower pole was split into two segments, but remained attached to the pedicle. There was a large amount of blood in the abdominal cavity; there was also a subserous hemorrhagic extravasation over almost the entire extent of the descending colon. This was believed to have had its origin from the splenic region and to have gravitated downward behind the peritoneal covering of the bowel. The patient died several days after operation. At necropsy the left renal artery was found to be partly torn across near the aorta, with the formation of a large retroperitoneal hematoma. The artery had become thrombosed, with consequent arrest of hemorrhage.

Aneurysm.—Mathé [18] reported a case of true aneurysm of the renal artery associated with nephrolithiasis, which was secondary to trauma; the condition was successfully relieved by nephrectomy.

Aneurysm of the renal artery is rare, only 56 cases having been reported in the literature. In 40 per cent of 55 cases reviewed there was a history of weakening and injury of the wall of the artery by trauma, and in the remainder a history of severe infections, producing lowered resistance due to sclerosis, fatty degeneration or inflammatory changes of the renal artery. This lesion is difficult to diagnose; only 7 of the reported cases were detected before operation or death. The chief symptoms are hematuria, pain and tumefaction. The hematuria is usually more sudden and more extensive than that caused by other renal lesions. Pulsation and systolic bruit, although rare, are pathognomonic signs. Renal aneurysm should be suspected if there is a ring-shaped, opaque area in the kidney.

The treatment of renal aneurysm is surgical, and operation should be performed as soon as this condition is suspected. Thirty-six untreated patients, whose cases have been reported, died; 16 of the 17 patients on whom nephrectomy had been performed survived. Resection of the aneurysm occasionally is possible. Plastic repair of the aneurysmal sac, drainage of the accompanying hematoma and other surgical procedures less radical than nephrectomy or excision give little, if any, relief.

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17. Edmunds, P. K.: Traumatic Rupture of Left Renal Artery Without Injury to Kidney, J. A. M. A. **99**:467 (Aug. 6) 1932.

18. Mathé, C. P.: Aneurism of the Renal Artery, J. Urol. **27**:607 (June) 1932.

Ptosis.—Braasch [19] stated that renal ptosis without urinary obstruction has no clinical significance and is seldom, if ever, the cause of symptoms. If obstruction exists as the result of ptosis, it can always be demonstrated by urographic or uroscopic examination, and operation is warranted only in the presence of such evidence. In the majority of cases in which nephropexy has been performed without definite evidence of urinary stasis, the symptoms will return within one or two years following operation. Urographic examination after operation is necessary to determine the permanence of a normal renal position as well as improvement in drainage. The percentage of patients having nephroptosis who can be relieved of their symptoms by renal fixation is comparatively small.

[COMPILERS' NOTE.—The recent tendency of American and European urologists again to perform renal suspension or fixation for movable or floating kidney has aroused much controversy. Aside from disputes over differences in various technics for the operation, of which there are many, there has been disagreement as to the indications for the operation. Most authorities believe that nephroptosis is a part of general visceroptosis. Kidd's bizarre concept of an Egyptian type of habitus associated with the condition is in line with this point of view.

Braasch has expressed the opinion of the conservative urologic element with regard to surgical indications in nephroptosis. Doubtless there are cases of floating kidney in which a spastic pelvis or ureter may give pain and in which fixation may bring relief. These, however, must be exceptional. It is well, in general, to take definite evidence of urinary stasis as the criterion for fixation of movable kidney.]

Pregnancy.—Farman and Gummess [20] stated that renal surgery during pregnancy entails a possibility of miscarriage of about 15 per cent, either immediately or before reaching full term. The mortality rate for all types of surgery, including operations on the kidney, during pregnancy is no greater than that for similar procedures in the nongravid state. Surgical intervention for renal lesions during pregnancy should be limited to cases in which it is necessary for the life or future health of the mother. The most common renal complications of pregnancy requiring operation are renal tuberculosis, calculous pyonephrosis, fulminating pyelonephritis and cortical abscess of the kidney.

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19. Braasch, W. F.: Conservation in the Treatment of Movable Kidney, J. A. M. A. **98**:613 (Feb. 20) 1932.

20. Farman, Franklin, and Gummess, K. C.: Surgery of the Kidney During Pregnancy: Report of Case, California & West. Med. **37**:94 (Aug.) 1932.

Foreign Body.—Waring and Drane [21] reported a case of an ascending foreign body in the pelvis of the kidney. The patient, a man, had pain in the right upper quadrant of the abdomen, fever, nausea and vomiting. Examination showed a shadow in the region of the right kidney and pyelonephritis. At operation a foreign body was removed from the right renal pelvis. The calculus was broken while being removed; it was found to be an encrustation of calcium and phosphate on a portion of seed-bearing grass. Several days later another portion of grass and stem was discharged from the wound. Recovery was uneventful. The patient had introduced the grass through the urethra, and a portion had slipped into the bladder. The authors are of the belief that during urination and contraction of the bladder the end of the foreign body was introduced into the ureter and that the sagittate arrangement of the seed on the stem caused it to work its way into the ureter.

Only 2 similar cases have been noted after questioning a group of urologists regarding this condition. Barney reported a case in which a calculus partially surrounding a toothpick was removed from the pelvis of the kidney. Braasch reported a case in which a stone on a hairpin was removed from the ureter; the hairpin had been introduced into the bladder.

Tumors.—Hand and Broders [22] reported an analysis of 193 cases of carcinoma of the kidney. There were 4 grades of malignancy, the basis of which depended on the degree of cellular differentiation in the carcinoma. The grade of malignancy was higher in patients less than 40 years of age. As the degree of malignancy increased, the duration of symptoms decreased; also, as the grade of malignancy increased, the length of postoperative life decreased. In cases in which malignancy was graded 2, 3 and 4, the average duration of life following operation was twice as long as the period over which symptoms existed; in cases in which the malignancy was graded 1, the average duration of life following operation was 3 times as long as the period over which the symptoms existed.

The technical difficulties in removing large carcinomas are important factors in determining immediate mortality. Infection and degeneration are common in large carcinomas. The fact that almost half of the patients operated on died before two years had elapsed makes questionable the advisability of surgical intervention in many cases in which the

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21. Waring, T. P., and Drane, Robert: An Ascending Foreign Body in the Kidney Pelvis, Am. J. Roentgenol. **28**:34 (July) 1932.

22. Hand, J. R., and Broders, A. C.: Carcinoma of the Kidney: The Degree of Malignancy in Relation to Factors Bearing on Prognosis, J. Urol. **28**:199 (Aug.) 1932.

carcinoma is large or fixed, or in which the general condition of the patient at the time of operation seems to be below par. Involvement of the renal veins by the carcinoma is a serious complication and increases the technical difficulties of the operation.

One hundred and forty-nine (77 per cent) of the 193 patients who underwent nephrectomy are dead; 44 (23 per cent) are living. Twenty-three (11.9 per cent) of the patients died in the hospital. Of the 126 patients who have died after leaving the hospital, 50 lived less than a year and 66 lived up to twenty-four months. Of the 149 patients who are dead, 97 died in the first five years and 16 died between the fifth and seventeenth years.

Hand and Broders concluded that study of the postoperative results in cases of carcinoma of the kidney, based on the degree of cellular differentiation in the tumor, represents a distinct advance in the knowledge of this disease.

[COMPILERS' NOTE.—Broders' principles of grading the index of malignancy in epithelial neoplasms, based chiefly on cellular differentiation, represent one of the outstanding contributions to pathology of the present day. It is quite natural that this prognostic criterion should be extended to epithelial neoplasms of the kidney, if the principle that lack of cellular differentiation or a preponderance of anaplastic cells in a growth predisposes to a more virulent and more rapid clinical course is sound. Hand and Broders found that there is a distinct clinicopathologic correlation between the grade of malignancy, operability and expectancy of life after operation. This conclusion is consistent with the facts recorded with regard to carcinoma of the skin, the rectum, the bladder and other sites which have been studied thus far.]

Ljunggren [23] stated that there has been considerable literature concerning the relation of tuberculosis to tumors, particularly to carcinoma. The majority of observers maintain that the coexistence of these conditions is only a coincidence. Others are of the opinion that some interrelationship exists between the two lesions: Either the tuberculosis is the primary condition, subsequent to which precarcinomatous changes and a malignant growth develop, or the tumor is the primary factor in the development of tuberculosis, through a lowered general resistance of the body to a tuberculous infection or through the tumor creating a point of lowered resistance in the affected organ.

Ljunggren described a case of tuberculosis and Grawitz' tumor in the same kidney. Seven similar cases have been reported in the literature. According to Ljunggren's point of view, the natural assumption is that it is a coincidence that the two conditions occurred simulta-

23. Ljunggren, Einar: Tuberculosis and Grawitz's Tumour of the Same Kidney, Acta chir. Scandinav. **69**:383 (March 3) 1932.

neously, but the possibility of a renal tumor predisposing to the development of the tuberculous process in the kidney should be taken into consideration.

Evans [24] reported the case of a woman, aged 36, with fibromyoma of the kidney. Symptoms had been present for four years. At operation the tumor was found to have no connection with the pelvic viscera; it was retroperitoneal, and its pedicle was attached to the capsule of the left kidney.

The growth was large and oval, measuring approximately 33 by 23 cm. The surface was roughened but not lobulated. There was a depression at one side, from the center of which radiating lines, resembling bundles of muscular fibers, extended over the surrounding surface. On section the tumor showed an external layer of solid tissue, about 0.5 cm. thick on one side and much thinner on the opposite side; it was pinkish gray and contained a definite nodule, about 1 cm. in length. The central part of the section consisted of a coarse honeycomb structure, the spaces of which were filled partly with mucus and clear fluid. Microscopic examination showed the growth to be a fibromyoma which had undergone extensive liquefactive degeneration.

Barney, Hunter and Mintz [25] stated that radiosensitive tumors described as lymphoblastoma and myeloblastoma are derived from the primitive cells of the lymph nodes, bone marrow and spleen. They are designated radiosensitive because of their response to roentgen rays or radium; for this reason surgery is generally not only contraindicated but futile.

Of 51 cases in which postmortem findings were studied in conjunction with clinical records, there were 39 cases of lymphoblastoma and 12 of myeloblastoma; in 83.3 per cent there were evidences of the disease in the genito-urinary tract.

In any case in which one or another of the tumors is suspected, careful and repeated studies of the blood smears should be made, as well as a careful examination for enlarged nodes, with a biopsy if necessary, and a roentgenologic examination of the chest and spine. The only rational treatment of these tumors is high-voltage roentgen therapy and, in some cases, external applications of radium. This treatment should be instituted as soon as possible after the diagnosis is made. Tumors of this type always cause fatal results. The length of life depends on the type of tumor, on the reaction of the patient to the tumor and on the involvement of vital organs such as the kidneys.

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24. Evans, Arthur: Fibromyoma of the Kidney, Proc. Roy Soc. Med. (Sect. Surg.) **25**:333 (Jan.) 1932.

25. Barney, J. D.; Hunter, F. T., and Mintz, E. R.: The Urologic Aspects of Radiosensitive Tumors of the Blood-Forming Organs, J. A. M. A. **98**:1245 (April 9) 1932.

[COMPILERS' NOTE.—Urologists may observe cases of tumors of the blood-forming organs because of a mass in the loin, pain in the back, retention of urine, pyuria, hematuria or priapism. Barney and his associates were among the first to emphasize how important it is for urologists to be ever watchful for tumors of the blood-forming organs when the foregoing signs are noted. The fact that some major involvement of the urinary tract was present in 83.3 per cent of the cases is significant.]

Waterworth [26] stated that giant unilateral renal calculi are rarely observed. Kreutzmann reported removal of a stone weighing 650 Gm., and found in the literature the report of a case cited by Mylvaganan in which a stone weighing 1,440 Gm. was removed at operation; the patient did not survive. The largest stone, weighing 1,130 Gm., was successfully removed by Morrison. Of the 8 cases in which there were unusually large renal calculi, cited by Kreutzmann, the smallest stone, weighing 339 Gm., occurred in the only female in the series.

Waterworth reported the case of a man, aged 64, who had renal pain of many years' duration. He had recently lost 20 pounds (9 Kg.), and a roentgenogram revealed a large, rounded shadow in the region of the right kidney. Nephrectomy was done; the kidney contained a squamous cell carcinoma and a stone 14.5 cm. in diameter and weighing 1,100 Gm. The calculus produced little if any disability in spite of a probable duration of twenty-eight years. The irritation caused by the presence of the stone for such a long time had resulted in the development of an epithelioma of the pelvis of the kidney which recurred following operation and ultimately resulted fatally.

[COMPILERS' NOTE.—A comparatively large number of cases of squamous cell tumors of the kidney, apparently developing secondarily to stones in the kidney, has recently been reported. In most of the cases, as in the one cited by Waterworth, the history suggests that the stones were present for a long time; the majority of the calculi were large and of the staghorn type. Oraison reported the case of a woman, aged 50, whose urinary trouble started with trauma when she was 24 years of age; for ten years preceding operation she had almost constant pain of a type suggesting stones in the kidney. Thomson-Walker cited the case of a man, aged 63, who had passed calculi at intervals for twenty-seven years. Darmady recently reported a case of squamous cell carcinoma in which hydronephrosis was present twenty-eight years before. The size, weight and striking lamellation of the calculus found at operation indicated that the latter had been present many years.

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26. Waterworth, S. J.: Giant Renal Calculus; Carcinoma of the Kidney Pelvis, J. Urol. **28**:77 (July) 1932.

A review of the reported cases apparently gives justification for suggesting that the majority of stones in the kidney should be removed as early as possible. This should be done not only to relieve pain and to prevent destruction of tissue of the kidney but, as described in the cases heretofore mentioned, to prevent formation of a malignant tumor.]

SUPRARENAL GLAND

Tumors.—Lazarus and Eisenberg [27] stated that tumors of the suprarenal gland are rare. From a clinical and pathologic point of view the most important growths are those arising from the epithelial part of the gland. The outstanding features of tumors involving the cortex are the associated changes in sexual characteristics, most frequently seen among girls. Because the suprarenal medulla is an offshoot of the sympathetic nervous system, tumors arising from this part of the gland bear a close resemblance to tumors of the sympathetic system.

Paraganglioma is composed entirely of mature chromaffin cells of the suprarenal medulla, is usually benign and, unlike other tumors of the suprarenal gland, occurs only in adults. Growths of the suprarenal gland tend to cause irreducible renal ptosis. Fever and cutaneous pigmentation are suggestive symptoms. The presence of a large, ovoid shadow in the roentgenogram, situated over a ptosed and rotated kidney, suggests a tumor of the suprarenal gland.

[COMPILERS' NOTE.—Paragangliomas are small tumors consisting of mature chromaffin cells. They are benign and are usually found at necropsy. Usually they are symptomless, the adrenogenital syndrome being absent, as in most suprarenal tumors originating in the sympathetic nervous system. Their occurrence only in adults is a striking contrast to other suprarenal tumors. Fever, cutaneous pigmentation, and the urographic finding of an ovoid tumor situated over a rotated and ptosed kidney are suggestive symptoms. The authors give an excellent review of tumors in general, their relative frequency of occurrence, their histogenesis and their relative malignancy.]

(To be concluded)

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27. Lazarus, J. A., and Eisenberg, A. A.: Tumors of the Adrenal Gland: Report of Two Cases of Paraganglioma of the Adrenal Gland, J. Urol. **27**:1 (Jan.) 1932.